The Chemistry on Diterpenoids in 1976

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Review

The Chemistry on Diterpenoids in 1976

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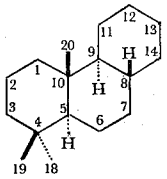
I. INTRODUCTION

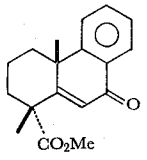
This is one of a series of our annual reviews[1] on diterpenoids chemistry. The classification of the compounds is the same as that which has been used in our reviews since 1969.

II. PODOCARPANE DERIVATIVES

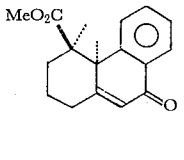


Podocarpane

Rearrangement of deisopropyl phenacylidene type diterpene by means of aluminum chloride was investigated. Thus, the reaction of **1** with aluminum chloride in anhydrous benzene gave the rearranged ester **2**, as a major product, in company



(1)



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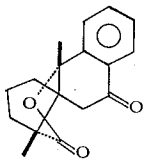

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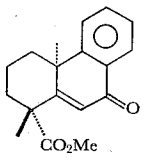

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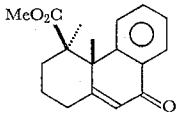

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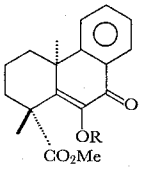
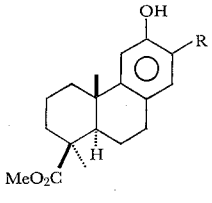


(6) R=Ac
(7) R=H



(8) R=H
(9) R=I

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with the γ-lactone **3**. On the other hand, the reaction of **4** afforded a large portion of the starting material in company with a small amount of the rearranged ester **5**. Next, the reaction of the enol acetate **6** gave only the enol **7** in the accompany of deacetylation[2]. Treatment of a phenol **8** with thallium (I) acetate and iodine gave a selective *ortho*-iodinated product **9**.[3]

N-Chloroacetylamine **10** on photolysis in methanol afforded the rearranged N-substituted glycine ester along with the unrearranged methyl ether.[4] (Chart 1)

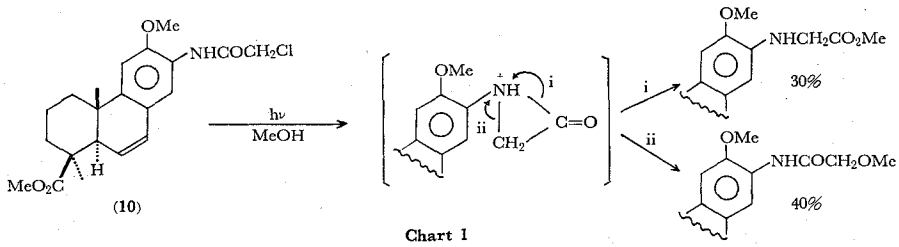
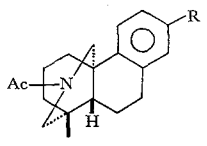
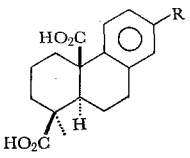


Chart 1

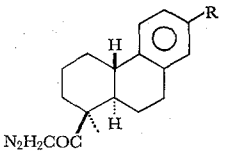
A new stereocontrolled synthetic route to some intermediates (**11a, b** and **12a, b**) for diterpenoid alkaloids and C_{20} gibberellins was published. The synthetic approach contains a novel method of angular alkylation based upon a regioselective intramolecular α-oxocarbenoid insertion across the benzylic C-H (at C-10) bond in the copper-catalyzed carbenoid decomposition of the easily accessible α-diazomethyl ketone **13a** and **13b** to the corresponding bridged tetracyclic ketones **14a** and **14b**.[5]



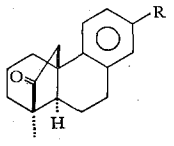
(**11a**) R=H
(**11b**) R=OMe



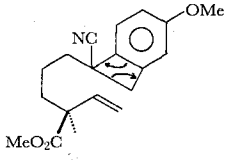
(**12a**) R=H
(**12b**) R=OMe



(**13a**) R=H
(**13b**) R=OMe



(**14a**) R=H
(**14b**) R=OMe



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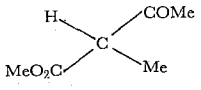

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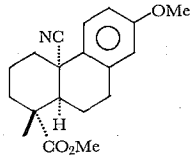

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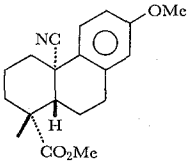

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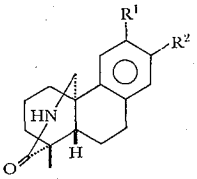
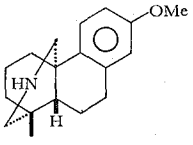


(**19**) R^1=H, R^2=OMe
(**21**) R^1=OMe, R^2=H



(20)

A facile regiospecific and stereocontrolled synthesis of a diterpene alkaloid intermediate from benzocyclobutenes was reported. Namely, thermolysis of **15** derived from methyl methylacetoacetate **16** in five steps gave phenanthrene derivative **17**, which was converted into the epimer **18** by oxidation, bromination, dehydrobromination, and hydrogenation. Catalytic reduction of **18** gave the lactam **19**, whose reduction with $LiAlH_4$ afforded imine **20**.[6] Similarly, compound **21** was synthesized.[7]

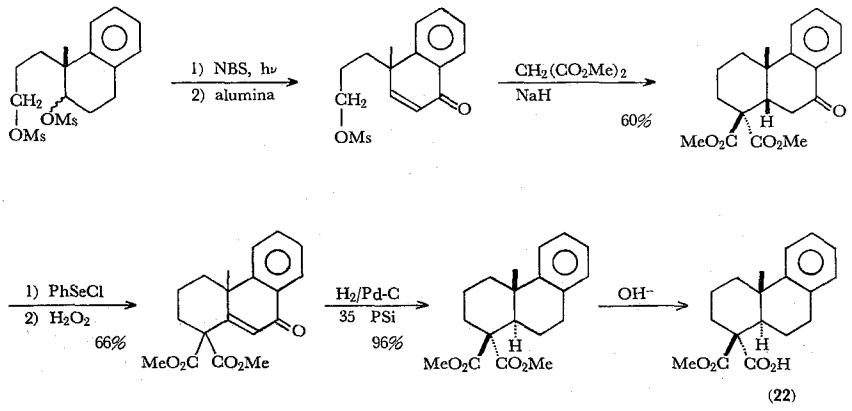
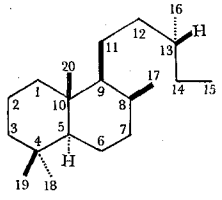


Chart 2

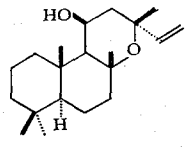
An efficient stereoselective synthesis of a tricyclic intermediate **22** for the synthesis of derivatives of abietic and podocarpic acid was reported.[8] (Chart 2)

III. LABDANE DERIVATIVES

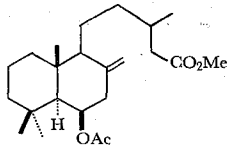


Labdane

11β-Hydroxymanoyl oxide (**23**) was isolated from *Juniperus oxycedrus* together with other diterpenes.[9] From *Cistus hirsutur*, methyl ester **24** of 6β-acetoxyladenic acid was isolated.[10] Labd-8(20), 13-dien-15-ol, (+)-manoyl oxide, epimanoyl oxide, *cis*-abienol, and 7α-hydroxydehydroabienol were isolated from the resin of



(23)



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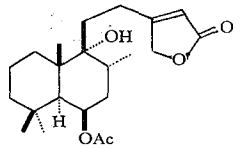
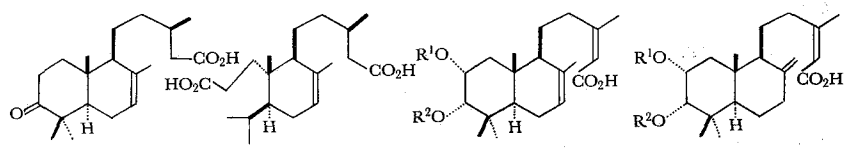


(25)

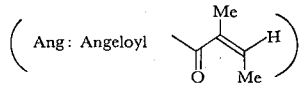
Pinus koraiensis and their identities confirmed by chemical and spectral methods.[11] A new diterpenoid, named vitexilactone, was isolated from the leaves of *Vitex cannabifolia* and its structure was established as **25** by the chemical and spectral examination.[12]

Several new diterpenes, **26**, **27**, **28**, **29**, **30**, and **31**, were isolated from the plants of the genus *Brickellia*. Compound **27** is a new type of degraded diterpene which, however, is closely related to **26**.[13]

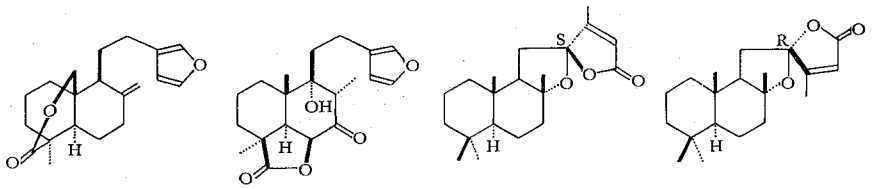
A new furanoid diterpene, potamogetonin (**32**), was isolated from seeds of *Potamogeton ferrugineus*. The structure was assigned on the basis of its spectral characteristics, particularly by NMR.[14] Structure of ballotinone, a diterpenoid from *Ballota nigra*, was established on the basis of its ^{13}C NMR spectrum to be 7-oxomarrubiin (**33**) [15, 16-epoxy-9-hydroxy-7-oxo-8βH-labda-13(16), 14-dien-19, 6β-olactone].[15] Giles and Schumacher[16] had proposed structures **34** and **35** for β- and α-levantenolide, respectively. However, it was reported that the C-12 stereochemistry of the α-levantenolide, $[\alpha]_D+60.4°$, should be changed to 12 S and that of β-levantenolide, $[\alpha]_D-59.6°$, to 12 R on the basis of their ^{13}C FT NMR spectra *etc.*[17]



(26) (27) (28) R^1=H, R^2=Ang (29) R^1=Ang, R^2=H (30) R^1=H, R^2=Ang (31) R^1=Ang, R^2=H



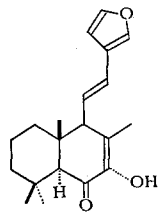
Ang: Angeloyl



(32) (33) (34) (35)

A furanoditerpene was isolated from *Hedychium spicatum*, and it was designated as 7-hydroxyhedychenone (**36**).[18] Five *ent*-labdane diterpenes were isolated from the neutral fraction of the resin of *Araucaria bidwilli*. Two of the compounds were the already known methyl *ent*-8β-hydroxy-labd-E-13-en-15-oate (**37**) and *ent*-8β, 15-labd-E-13-enediol (**38**). Three of them, previously unknown, were assigned the structures *ent*-15-acetoxy-labd-8, E-13-diene (**39**), *ent*-labda-8, E-13-dien-15-ol (**40**) and methyl *ent*-8α-hydroxy-labd-E-13-en-15-oate (**41**).[19]

A new diterpene galactoside, named acanthospermol-β-galactosidopyranoside, was isolated from *Acanthospermum hispidum* and its structure (**42**) was clarified.[20] 13-Epimanool was isolated from *Pinus contorta* bark and *Tsuga heterophylla* wood. Southern pine (*Pinus* spp.) tall oil was found to contain a mixture of manool and 13-epimanool.[21]



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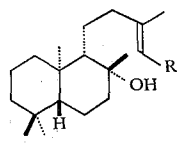
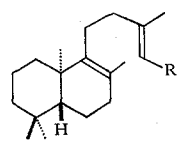
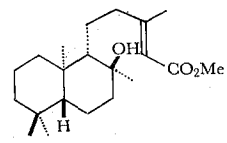


(37) R=CO_2Me
(38) R=CH_2OH



(39) R=CH_2OAc
(40) R=CH_2OH



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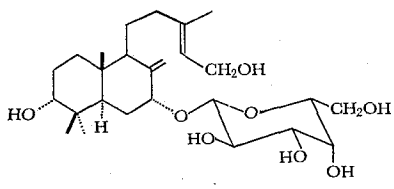

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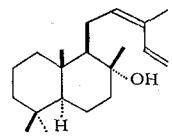

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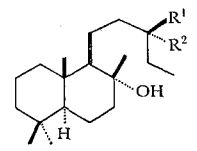
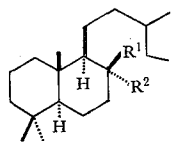
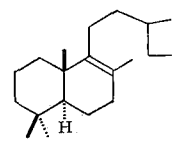


(44) R^1=Me, R^2=H
(45) R^1=H, R^2=Me

It was shown that tetrahydroabienol, which was obtained by hydrogenation of abienol (**43**), was a quasiracemic compound formed from C-13 epimers. Namely, the compound is a mixture of **44** and **45**.[22] The tetrahydroabienol (**44** and **45**) with phosphorus pentachloride smoothly gave the chloride **46** with less than 5% elimination to olefinic compounds. On the other hand, the C-8 epimeric alcohol **48** with phosphorus pentachloride gave a mixture comprising chloride **47** (40%), chloride **46**, and olefin **49**.[23]



(46) R^1=Me, R^2=Cl
(47) R^1=Cl, R^2=Me
(48) R^1=OH, R^2=Me



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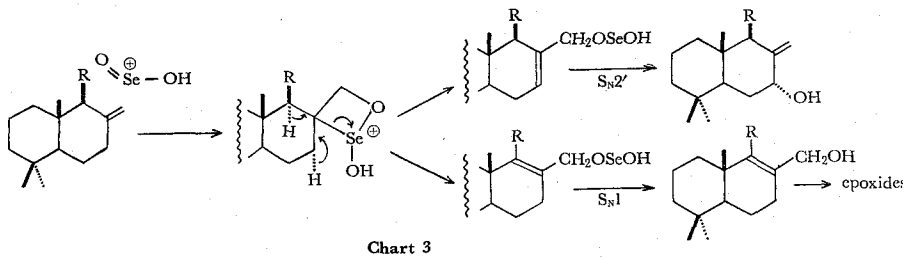


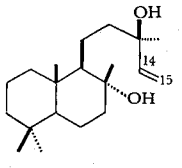
Chart 3

Allylic oxidation of exocyclic olefins with SeO_2/H_2O_2 was investigated and the mechanism was postulated: the reaction would proceed through the intermediacy of an oxaselenocyclobutane to a selenite ester which is solvated by competitive unimolecular (S_N1) and bimolecular (S_N2') processes.[24] (Chart 3)†

† See another mechanism by H. P. Jensen and K. B. Sharpless (*J. Org. Chem.*, **40**, 264 [1975]).

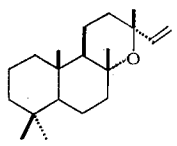
In the synthesis of tertiary azides from sclareol **50** and dihydrosclareol **51**, NH_3/BF_3-Et_2O was used. Stereoselective introduction of an azide group at C-8 was observed under appropriate conditions. Manoyl oxide **52** and 13-epimanoyl oxide **53** provided azide-ketone **54** by vinylic fragmentation with loss of C-14 and C-15.[25]

The action of NaN_3-ICl or $TlOAc$-I_2 on labd-8(17)-en-13-ol **55** was investigated. The former reagent gave a mixture of **56** and **57**, while the latter gave a mixture of **56** and **58**.[26]



(50)

(51) 14, 15-dihydro-derivative



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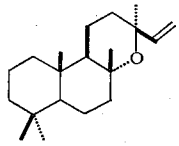

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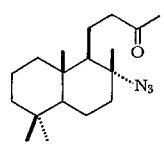

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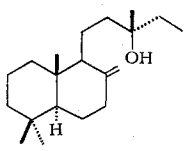

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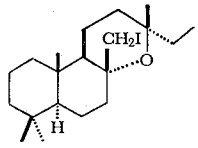

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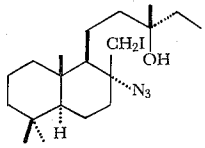

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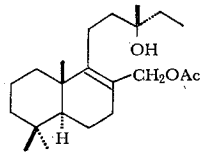
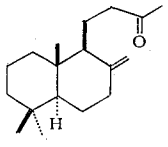


(58)

Photochemical reaction of 15,16-dinorlabd-8(17)-en-13-on **59** was investigated. Namely, UV irradiation of **59** led to the fragmentation product **60** and its photocyclization product **61**. Ethers **62** and **63** and β,γ-unsaturated alcohols **64** and **65** were formed *via* ketone **66**.[27] A partial synthesis of methyl lambertianate **67** from 13-keto degradation product **68** of methyl agathate was reported.[28]



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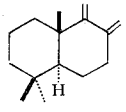

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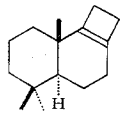

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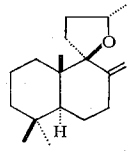

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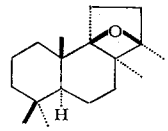

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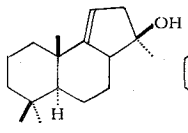

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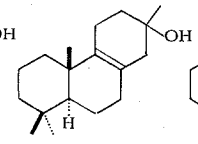

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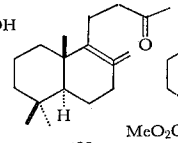

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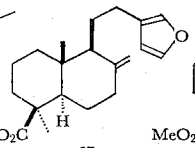

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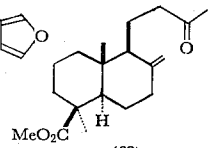


(68)

α- and β-Levantenolide (**34** and **35**) were synthesized using functionalization at C-12 of labdanolic diterpene as shown Chart 4.[29]

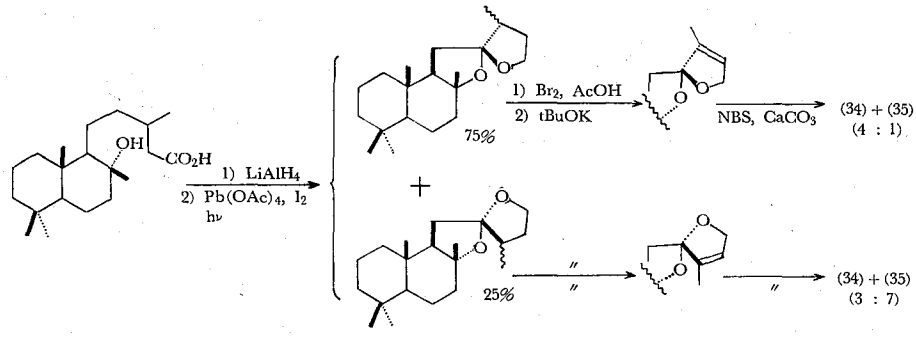


Chart 4

A synthesis of grindelic acid (**69**) from the easily available unsaturated (+)-ketone **66** was reported.[30] The sequence is shown in Chart 5.

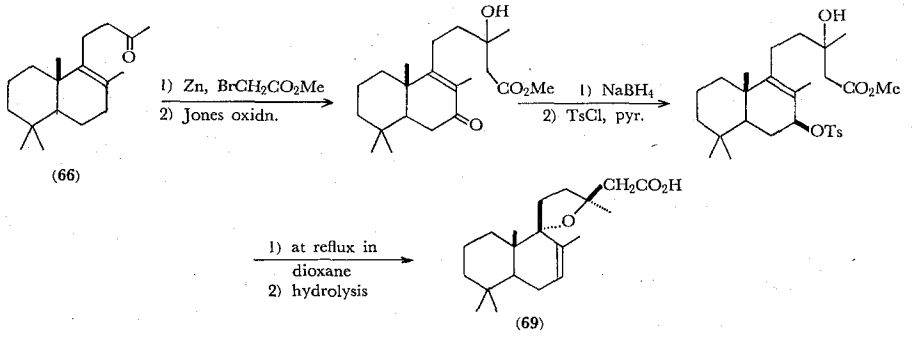


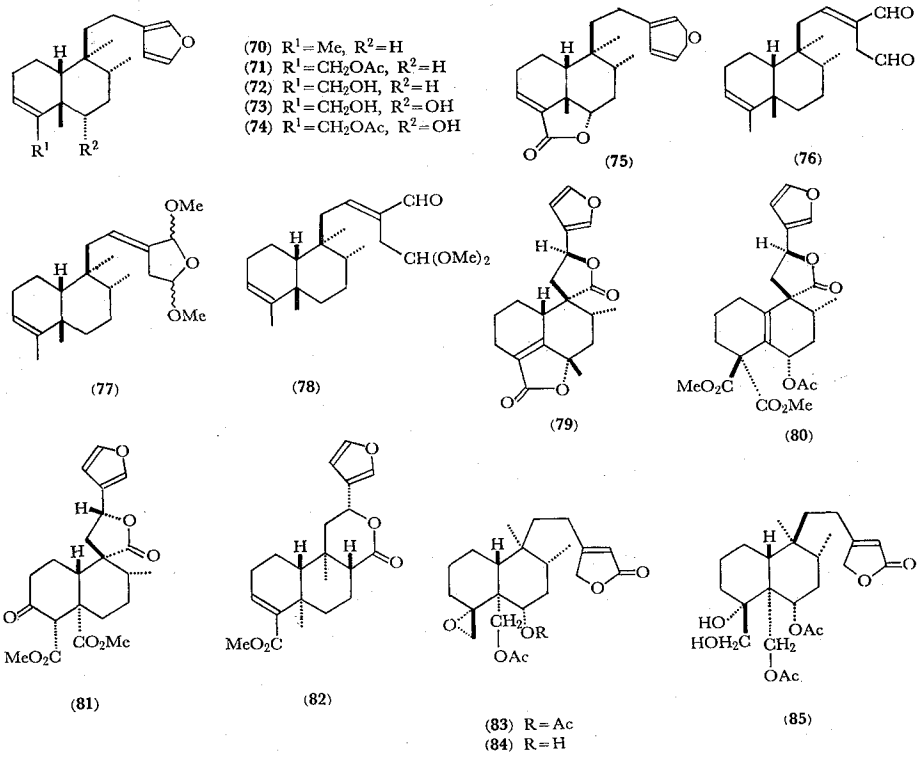
Chart 5

Isolation of labdane type diterpene from *Pinus-pumila* resin was reported,[31] but the details are not known.

IV. CLERODANE DERIVATIVES

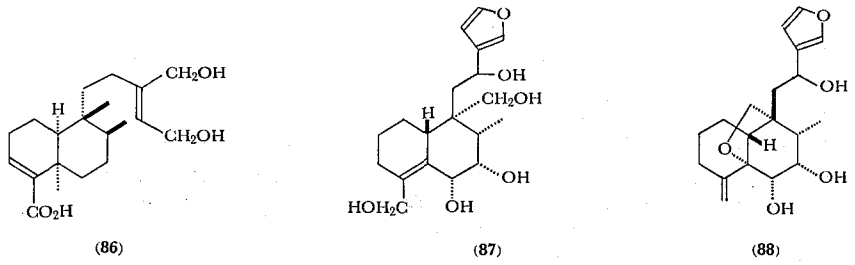
Six new diterpenoids, (**70-75**) were isolated from the roots of *Solidago arguta*, and their structures were deduced from their chemical and spectral properties.[32] A new diterpene dialdehyde named linaridial was isolated from *Linaria japonica*, and the structure was established as **76** on the basis of the physicochemical evidence and the chemical correlation with the known furanoclerodane type compound **70**. At the same time, two linaridial-analogs (**77** and **78**), which seem to be the artefacts formed secondarily from linaridial (**76**), were isolated from methanol extract of the same plant.[33] Two lactones, mallotucin A and B, were isolated from *Mallotus repandus*.[35] Mallotucin A was found to be identical with teucvin (**79**) isolated from *Teucrium viscidum var. Miquelianum*.[34] Mallotucin B (**80**) was found to be the first diterpenoid with geminal methoxycarbonyl groups.[35]

The structure and stereochemistry of corylifuran, a clerodane type diterpene from *Croton corylifolius*, have been determined as **81** by chemical and spectroscopic



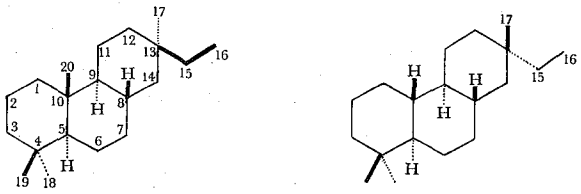
data and X-ray crystallographic analysis.[36] Methyl barbascoate (**82**), a major diterpenic component of the medicinal plant *Croton californicus*, was isolated and the structure determined by a combination of spectral and X-ray crystallographic studies.[37] The structures of Ajugarin-I, II, and III (**83**, **84**, and **85**), which are insect antifeedants, isolated from *Ajuga remota* leaves, were determined[38]

A new clerodance type diterpene, floridiolic acid (**86**), was isolated from *Evodia floribunda* and the structure was confirmed by X-ray analysis of its methyl ester.[39,40] Diterpene pentol **87**, obtained by reduction of teucrin A with $LiAlH_4$, on treatment with 5% H_2SO_4 underwent an anisotropic rearrangement to give **88** identified by its acetates, acetonide, and oxidation products.[41]



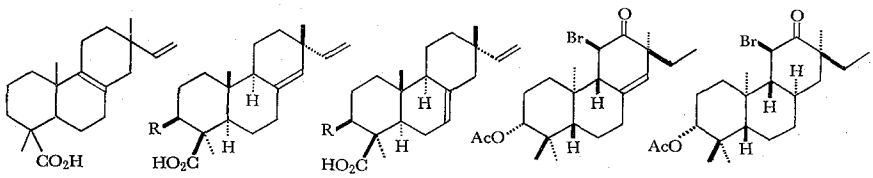
A review on the insect antifeedants found in plants was published. Several clerodane-type diterpenes were described in it.[42]

V. PIMARANE AND ISOPIMARANE DERIVATIVES



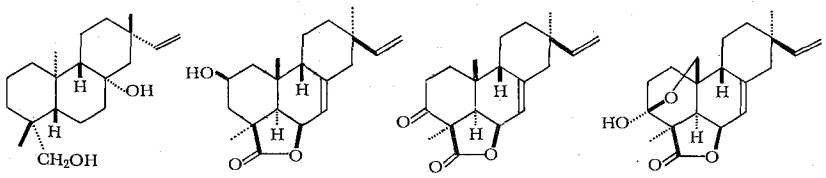
Pimarane and Isopimarane

Two diterpene acids, neothujic acid III and IV, were isolated from the fertilized female strobiles of thuja, *Thuja occidentalis*. The structure of neothujic acid III was determined as **89**.[43] Four new pimarane type diterpene acids (**90**, **91**, **92**, and **93**) were isolated from *Dimorphotheca pluvialis*[44] together with a beyerane type diterpene acid. The X-ray analyses of *ent*-3β-acetoxy-11α-bromoisopimar-8(14)-en-12-one (**94**) and its dihydroderivative (**95**) were reported.[45,46]



(**89**) (**90**) R=H, (**91**) R=OAc, (**92**) R=H, (**93**) R=OAc, (**94**), (**95**)

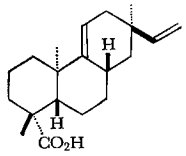
(−)-Thermarol (**96**), a new *ent*-pimarane-type diterpene diol was isolated together with *ent*-pimara-8(14), 15-dien-19-oic acid and *ent*-pimara-8(14), 15-dien-19-ol from *Jungermannia thermarum*.[47] Structure **97** of momilactone-C, a minor constituent of growth inhibitors in rice husk, was determined by X-ray analysis, which revealed that C-9, C-10 linkage of **97** was unusual *cis* configuration having a boat conformation of the ring A. The stereochemistry of C-9 of previously reported momilactone-A and B has been erroneously written and should now be revised to β-configuration (**98** and **99**) with respect to hydrogen atom as in momilaction-C.[48]



(**96**), (**97**), (**98**), (**99**)

A new pimaradiene carboxylic acid **100** was isolated from *Othonna cylindrica* as its methyl ester.[49] The structure **101** for the γ-lactone derived from acid treatment of dihydroisopimaric acid (**102**) was revised to be **103** with a *cis*-A/B ring fusion, which was based on ^{13}C NMR chemical shift data and spin-lattice relaxation time (T_1) measurements.[50] Constitutional effects in chemical ionization mass spectrometry of di- and tri-functional isopimarane type diterpens were reported.[51] The acid–

catalyzed reactions of 7α, 8α-epoxy-isopimar-15-ene (**104**) and 7β, 8β-epoxyisopimar-15-ene- (**105**) were described. The epoxides were allowed to react with boron trifluoride etherate in dry benzene to give compounds **106**, **107** and/or **108** with some miscellaneous products.[52]



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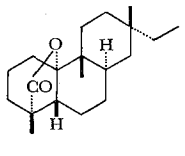

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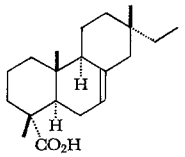

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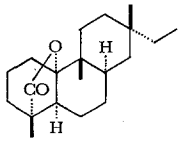

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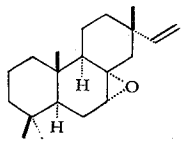

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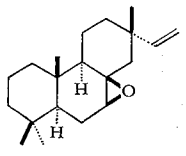

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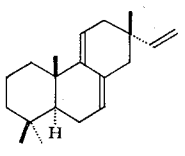

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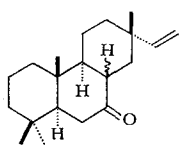

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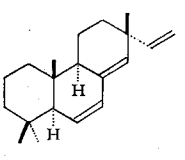

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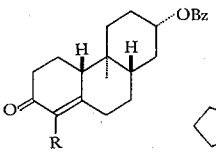
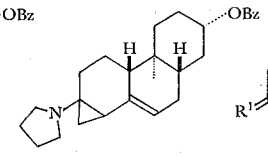


(109) R=Me
(110) R=H



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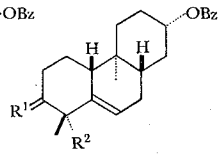
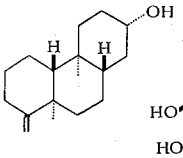


(112) R^1=O, R^2=CO_2Et
(113) R^1=H_2, R^2=CO_2H



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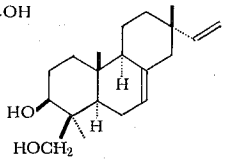
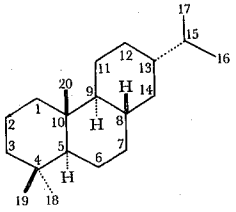


(115)

An intermediate **109** in the synthesis of erythroxydiol X was prepared by methylation of **110** *via* its enamine derivative. Thus, the pyrrolidine enamine on treatment with diazomethane to give the cyclopropaphenanthrene **111** which was hydrolyzed to **109** by heating in aq. MeOH.[53] Furthermore, alkylation of **109** with $ClCO_2Et$ gave the ester **112** which was converted to the acid **113** by Clemmensen reduction followed by hydrolysis.[54] The perhydrophenanthrenol **114** was prepared from **110** in 9 steps.[55] Formulae **109-114** represent their racemate, respectively.

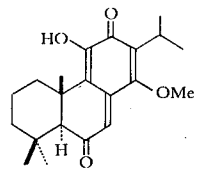
In a review on the biosynthetic studies with ^{13}C labeled precursors, virescenol B (**115**) was exemplified.[56]

VI. ABIETANE DERIVATIVES

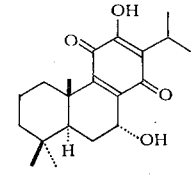


Abietane

From *Hyptis fructicosa*, 14-methoxytaxodione **116** was isolated together with the known horminone **117** and its structure was determined on the basis of spectroscopic data and by chemical correlations.[57] Two new diterpenoid quinones, conacytone (**118**) and icetexone (**119**) were isolated from *Salvia ballotaeflora*. Their structures were determined by the X-ray analyses.[58,59] The acentric crystal structure of *cis*-coleon D (**120**) was established by the X-ray analysis (by direct methods). The absolute configuration was determined from the known chirality of the A/B ring junction.[60] Isolation of stemolide (**121**), a novel diterpene bisepoxide, from the leaves of *Stemodia maritima* was reported. The structure was determined by X-ray analysis.[61] Two alcohols isolated from *Nepeta granatensis* were identified as 7α, 18-dihydroxy-14-abietene and 14α, 18-dihydroxy-7-abietene by their chemical reaction.[62]



(116)



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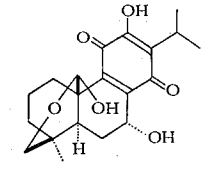

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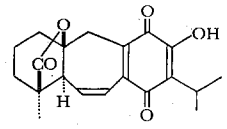

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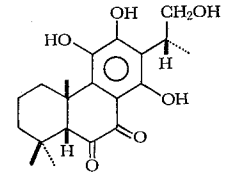

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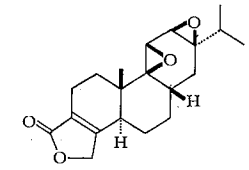
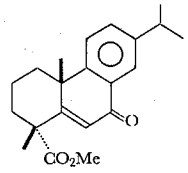
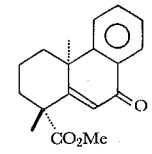


(121)

Kinetics of the thermal isomerization of abietic acid in the presence of air at 200° into palustric and neoabietic acid was investigated.[63] Iodine catalyzed disproportionation of abietic acid gave dihydroabietates or dehydroabietates. E.s.r. meas-



(122)



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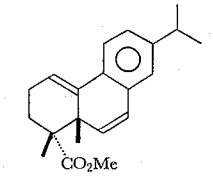

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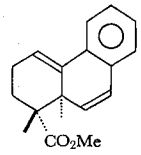
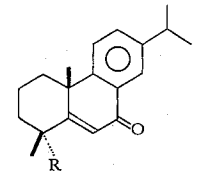
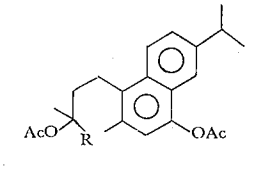


(125)



(126) R=Me
(127) R=CH_2OAc



(128) R=Me
(129) R=CH_2OAc

urements suggested the intermediacy of free radicals.[64] Acid treatment in acetic anhydride of blocked cyclohexadienone derivatives **122** and **123** gave **124** and **125**, respectively, through Wagner-Meerwein rearrangement of the angular methyl group. On the other hand, under similar conditions, **126** and **127** were transformed into **128** and **129**, respectively, as the result of an abnormal dienone phenol rearrangement.[65]

Direct introduction of bromine into the ring A of phenacylidene derivatives of *l*-abietic acid was developed and it was applied to the conversion of abietic acid into teideadiol (**130**) having a hydroxy group on the ring A of its abietane skeleton.[66] (Chart 6)

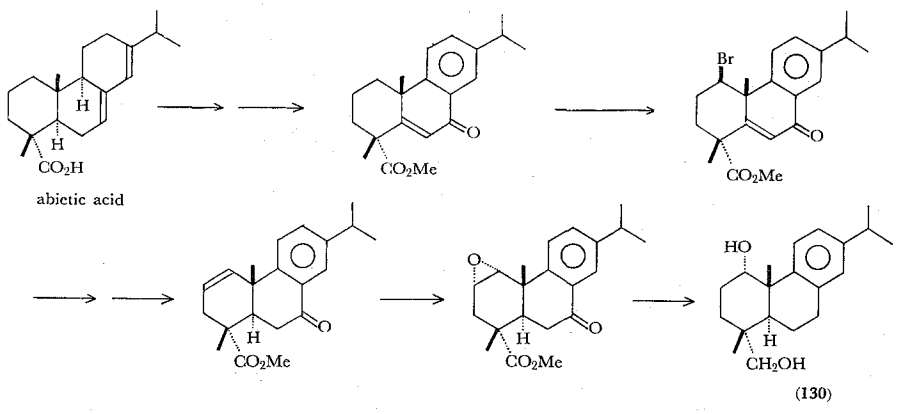
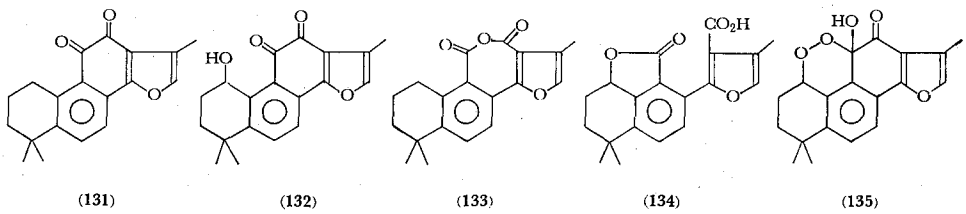


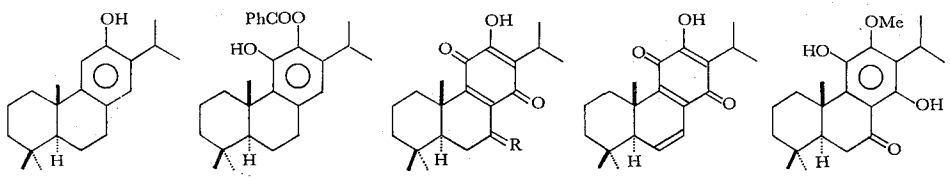
Chart 6

Photo-oxidation of tanshinone II (**131**) was published. Thus, UV irradiation of **131** in the presence of air afforded 9-hydroxy-tanshinone (**132**), anhydride **133**, and lactone **134**. The formation of these compounds was explained in terms of an intermediate **135**, derived from tanshinone II by photoenolization and oxygenation.[67]

Oxidation of ferruginol **136** with benzoyl peroxide gave 12-benzoyloxy-11-hydroxyabieta-8, 11, 13-triene (**137**) which was converted into taxoquinone (**138**), 7α-acetoxyroyleanone (**139**), dehydroroyleanone (**140**), horminone (**117**), 7-oxoroy-



(131) (132) (133) (134) (135)



(136) (137) (138) R=α-H, β-OH (139) R=α-OAc, β-H (141) R=O (140) (142)

leanone (**141**), and inuroyleanone (**142**).[68]

Transformation of dehydroabietic acid (**145**) to a key intermediate for the synthesis of steroids was examined. 13-Isopropyl-18, 19-bisnor-5β-podcarpa-8, 11, 13-trien-3-one (**143**) was synthesized from **145** *via* the ketone **144**.[69] In addition, methyl 14-oxo-podocarpan-18-oate **146** was synthesized from **122**.[70]

A potential synthetic intermediate **147** of *rac*-carnosic acid **148** was synthesized as shown in Chart 7.[71]

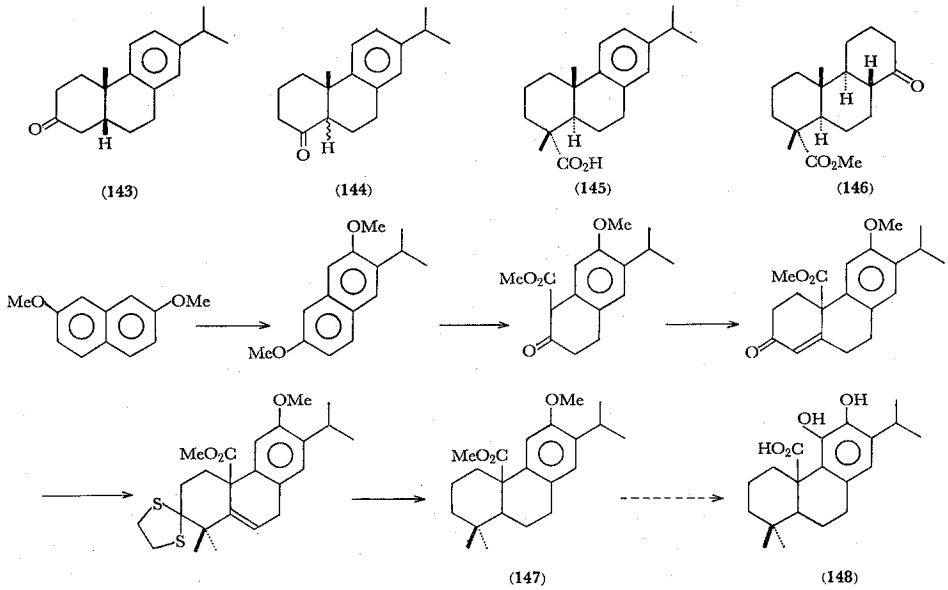


Chart 7

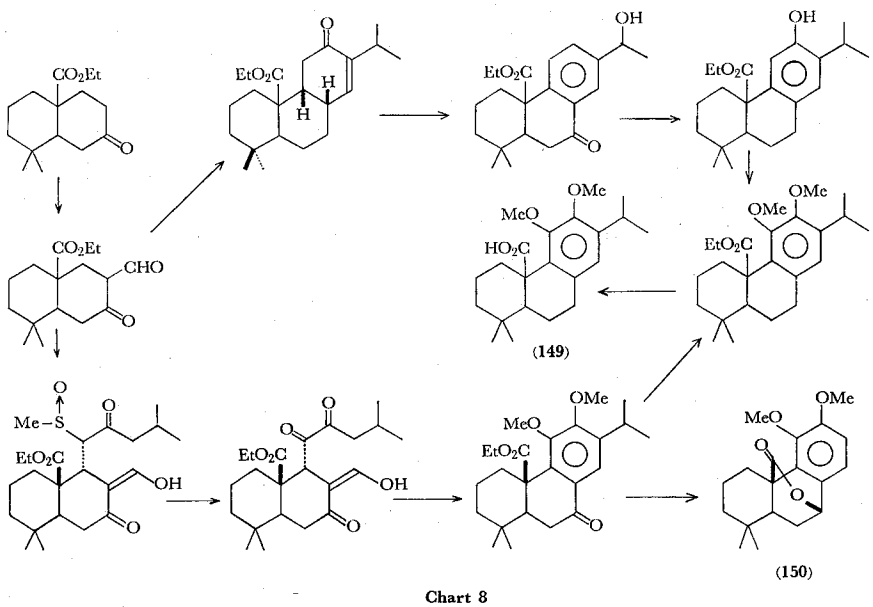
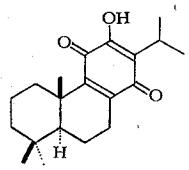


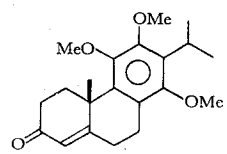
Chart 8

The total syntheses of *rac*-carnosic acid dimethyl ether (**149**) and *rac*-carnosol dimethyl ether (**150**) were achieved.[72] The outline is shown in Chart 8.

rac-Royleanone (**151**) was prepared in 16 steps from 2,3,6-trimethoxybenzoic acid *via* the trimethoxy intermediate **152**.[73]

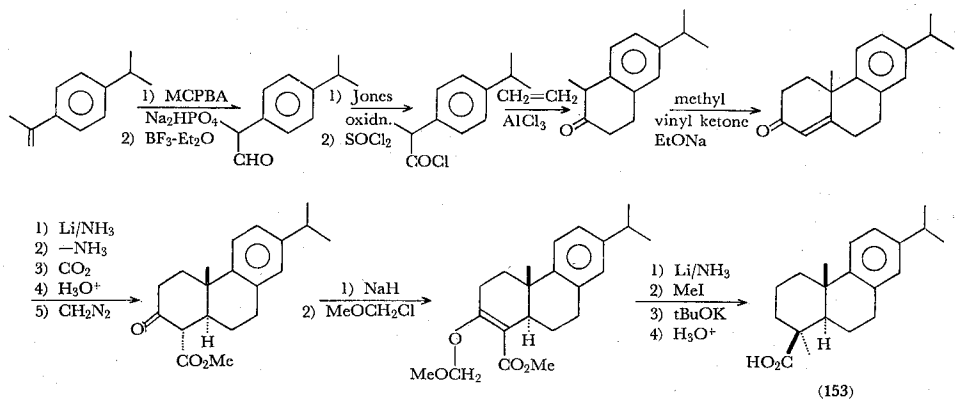


(151)



(152)

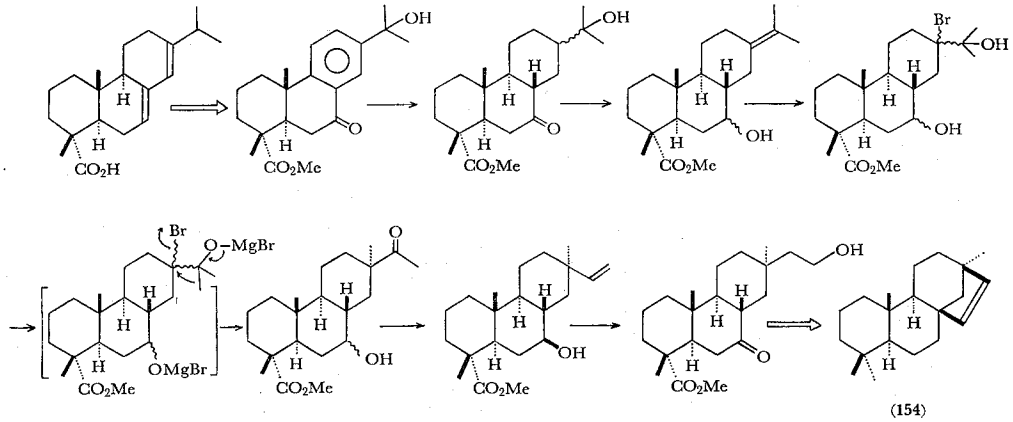
A short and highly stereoselective total synthesis of *rac*-callitrisic acid (**153**) was described.[74] The sequence is shown in Chart 9.



(153)

Chart 9

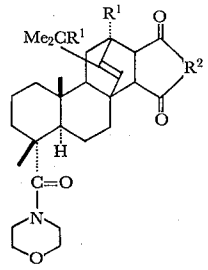
Stereoselective isopropyl-methyl migration in *l*-abietic acid derivative was investigated, and was applied to synthesis of 15-beyerene (*l*-hibaene) (**154**) from *l*-abietic acid as shown in Chart 10.[75]



(154)

Chart 10

Synthesis of deuterium and tritium labeled derivatives (**155** and **156**) of moleopimaric acid was reported.[76]

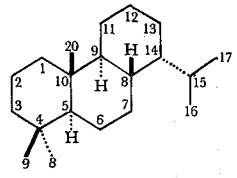


(155) $R^1={}^2H$ or ^3H, $R^2=O$
(156) $R^1={}^2H$ or ^3H, $R^2=NCH_2CH_2OH$

Effects of hydrofluorene and hydrophenanthrene compounds derived from dehydroabietic acid (**145**) on the second leaf sheath growth of rice seedlings were examined in the presence and absence of gibberellic acid.[77]

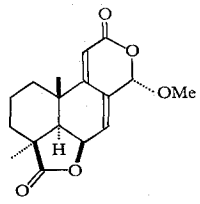
A review on the synthetic chemistry starting from abietic acid was published.[78]

VII. TOTARANE DERIVATIVES

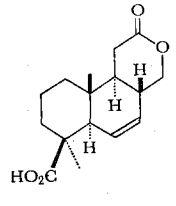


Totarane

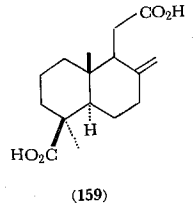
Three new C_{16} terpenoids, which may lie on the biosynthetic pathway for the antifungal metabolite LL-Z 1271α (**157**), were isolated from an *Acrostalagmus* fungus, and assigned the structures **158**, **159**, and **160**.[79] The compound **157** has been assumed to be derived from diterpene biogenetically.[80]



(157)



(158)



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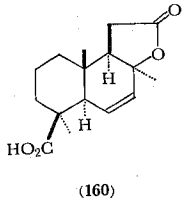

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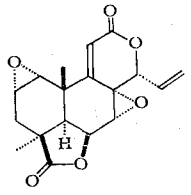
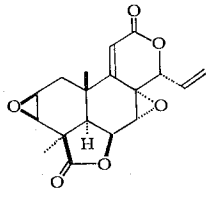
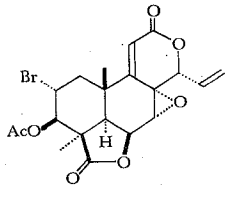


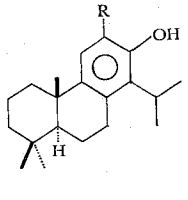
(161)



(162)



(163)

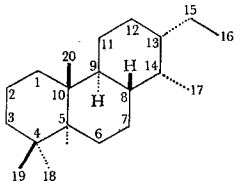


(164) R=H
(165) R=I

The previously published structure **161** of sellowin B was revised to **162** on the basis of the X-ray crystallographic study of its bromohydrin acetate **163**.[81] Treatment of **164** with thallium (I) acetate and iodine gave **165**.[3]

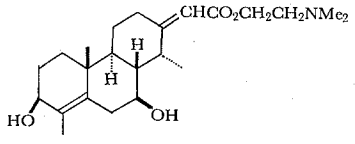
The chemistry of biologically active norditerpene dilactones isolated from *Podocarpus* species was discussed.[82]

VIII. CASSANE DERIVATIVES

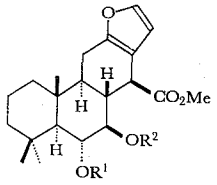


Cassane

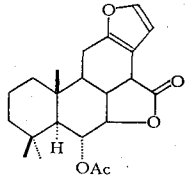
19-Nor-4-dehydrocassaidine (**166**) was isolated from the bark of *Erythrophleum couminga* and its structure was determined by spectral data.[83] Investigation of diterpenoids in four species of *Pterodon* was carried out. From *P. pubescens*, the new ester **167** was isolated. From *P. emarginatus*, compounds **168**, **169**, **170**, and **171** were isolated. The diterpenoids **169** and **170** were isolated also from *P. polygalaeflorus*. The compound **170** was further isolated from *P. appariciοi*.[84]



(166)

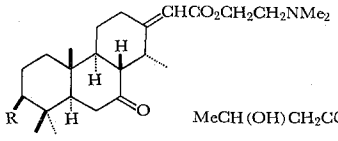


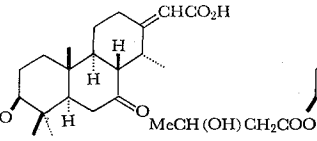
(167) $R^1=R^2=Ac$
(169) $R^1=R^2=H$
(170) $R^1=Ac$, $R^2=H$
(171) $R^1=H$, $R^2=Ac$



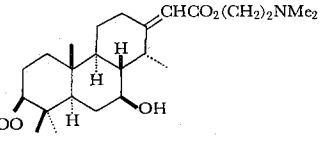
(168)

From cassaine (**172**), several analogs, (**173-179**) were prepared. From 3-dehydrocassaic acid (**180**), derivatives **181** and **182** were made.[85]



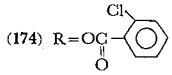


(178)



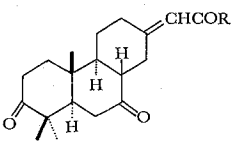
(179)

(172) R=OH
(173) R=OCOCH$_2$CH$_2$Cl

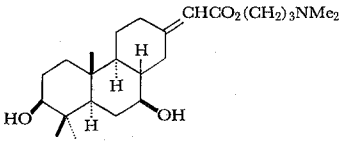


(174) R=

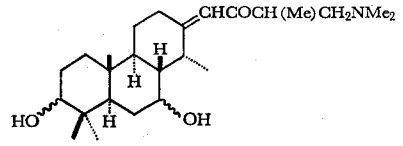
(175) R=OCOCH=CMe$_2$
(176) R=OCOCH$_2$COMe
(177) R=OCOCH$_2$CH(OH)Me



(180) R=OH
(182) R=NHCH$_2$CH$_2$NMe$_2$



(181)



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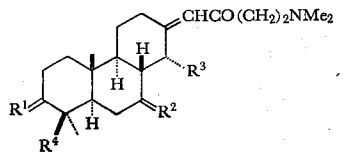
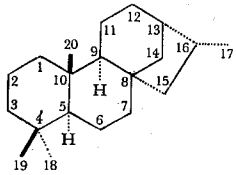


(184) R^1=O, R^2=H_2, R^3=H, R^4=Me
(185) R^1=H_2, R^2=O, R^3=Me, R^4=CO_2Me

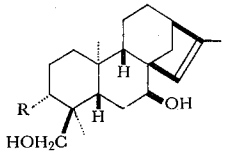
Compounds **183**, **184**, and **185** were prepared from the known derivatives of cassenic acid, and **183** and **185** were shown to have cardiotonic activity.[86]

IX. KAURANE DERIVATIVES

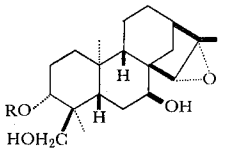


Kaurane

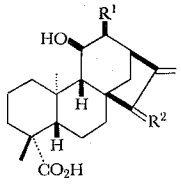
From *Sideritis paulii*, sideridiol (**186**), isofoliol (**187**), and a new diterpene, epoxyisofoliol (**188**) were isolated.[87] A new diterpenoid, epoxyisosidol (**189**) was isolated from *Sideritis biflora*.[88] Four new hydroxylated *ent*-kauran-19-oic acids, **190**, **191**, **192**, and **193** were isolated from *Eupatorium album*.[89]



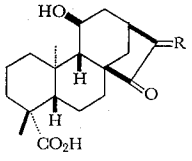
(186) R=H
(187) R=OH



(188) R=H
(189) R=Ac

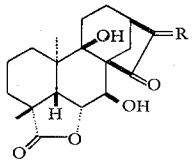


(190) R^1=H, R^2=α-H, β-OH
(191) R^1=H, R^2=O
(192) R^1=OH, R^2=α-H, β-OH

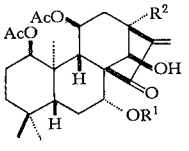


(193) R=α-H, β-Me
(194) R=α-Me, β-H

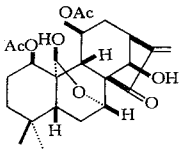
From *Pteris dispar*, **191** and four new diterpenes, **193**, **194**, **195**, and **196** were isolated.[90] Eight new diterpenes, rastronols A (**197**), B (**198**), C (**199**), D (**200**), E (**201**), F (**202**), G (**203**), and H (**204**), were isolated from *Englerstrum scandens*.[91]



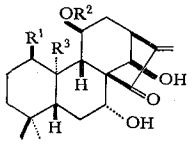
(195) R=CH_2
(196) R=α-H, β-Me



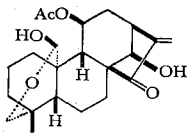
(197) R^1=R^2=H
(198) R^1=H, R^2=OH
(199) R^1=Ac, R^2=OH



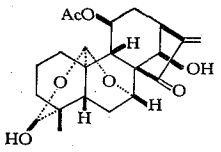
(200)



(201) R^1=OH, R^2=H, R^3=CHO
(202) R^1=H, R^2=Ac, R^3=CH_2OH



(203)

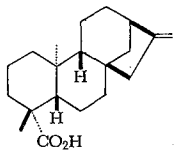


(204)

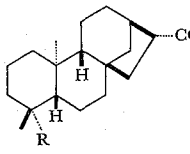
ent-Kaur-16-en-19-oic acid (**205**) was isolated as its methyl ester from *Othonna cylindrica*.[49] The root bark of *Annona senegalensis* is used by Nigerian herbalists to treat cancer. From the root bark of this plant, six crystalline materials were isolated. They were found to be *ent*-kauran-16β-ol, *ent*-kaur-16-en-19-oic acid (**205**), methyl *ent*-16α-kauran-19-al-17-oate (**206**), methyl *ent*-19-nor-16α-kauran-4β-ol-17-oate (**207**), compound **208**, and **209** or **210**.[92]

The root and overground part of *Verbesina angustifolia* were found to contain diterpenic acids **205** and **211**. The root of *V. oncophora* also contained these two acids and *ent*-kauran-13-ol.[93]

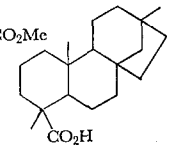
A new diterpenic acid **212** was isolated from *Melampodium perfoliatum*.[94] The "coffee atractylosides" **213** and **214** were isolated from *Coffea arabica*.[95]



(205)



(206) R=CHO
(207) R=OH



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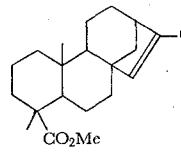

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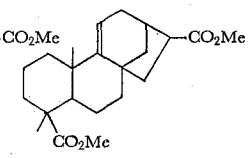

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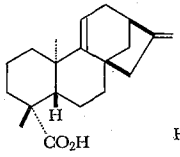
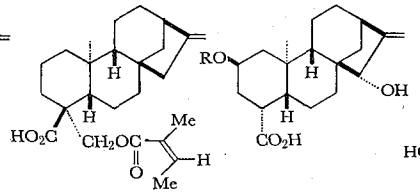
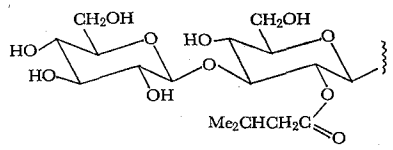


(211)

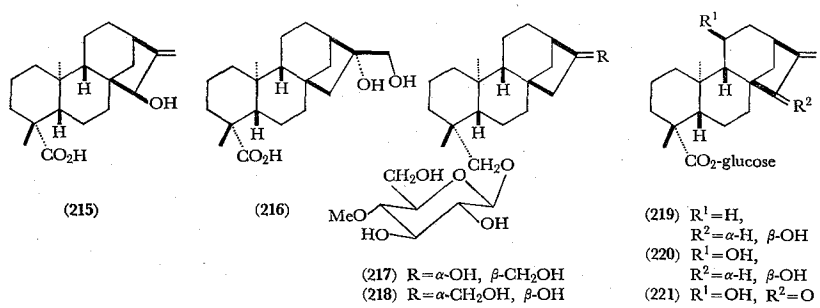


(212)

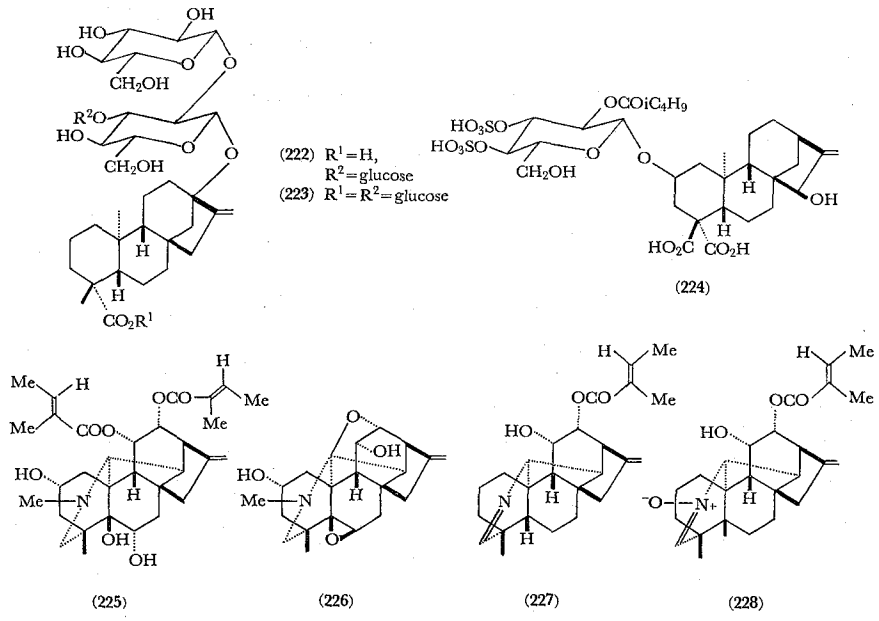
(213) R=glucose
(214) R=



The enzymatic hydrolysis of the glycosides fraction of the leaves of *Stevia paniculata* gave four aglycones and their structures were elucidated as **190**, **191**, **215**, and **216**.[96] Two new diterpene-glycosides, microlepin and 16-epimicrolepin, were isolated from the overground part of *Microlepia marginata* and assigned the structures **217** and **218**.[97] The structures of paniculosides, I, II, and III, three new diterpene-glycosides of *Stevia Paniculata*, were determined as **219**, **220**, and **221**.[98]



From the leaves of *Stevia rebaudiana*, two new sweet glucosides, rebaudiosides A and B, were isolated besides the known glucosides, stevioside and steviolbioside. On the basis of IR, MS, ^{1}H and ^{13}C NMR as well as chemical evidence, the structures **222** and **223** were assigned to rebaudiosides A and B, respectively.[99] Isolation and identification of the hypoglycemic agent, carboxyatractylate (**224**), from *Xanthium strumarium* were reported.[100]

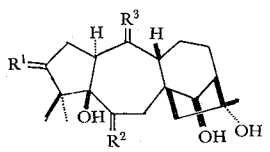


Anopterine was isolated from the leaf and bark of *Anopterus macleayanus* and bark of *A. glandulosus*, and its structure was determined to be represented as **225**. Hydrolysis of anopterine and oxidation with potassium ferricyanide gave an unusual product **226**, whose structure was confirmed by the X-ray analysis.[101,102] To two new minor alkaloids of *A. macleayanus*, anopterimine and anopterimine N-oxide, were assigned the structures **227** and **228**, and the partial structures of two other new alkaloids, hydroxyanopterine and dihydroxyanopterine were also reported.[103]

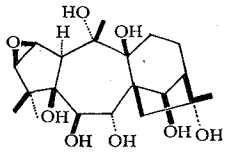
The structures of grayanotoxins XVI and XVII, two physiologically active diterpenoids of *Leucothoe grayana*, were elucidated as **229** and **230**.[104] On the basis of the

results of an X-ray analysis the stereochemisty of pieristoxin G (**231**) was discussed.[105]

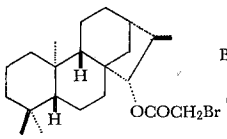
The ^{13}C NMR spectra of some kauranoid diterpenes have been assigned. The application of the results to the determination of the sites of hydroxylation in this series was discussed.[106] The X-ray analyses of **232**[107] and **233**[108] were reported. The reaction of the keto esters **234** and **235** with Na in liquid ammonia afforded mixtures of *ent*-kaurane, *ent*-beyerane, and dimeric products.[109]



(229) R^1=α-H, β-OH, R^2=α-H, β-OAc, R^3=CH_2
(230) R^1=R^2=O, R^3=α-OH, β-Me



(231)



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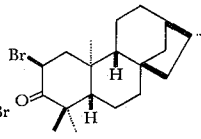

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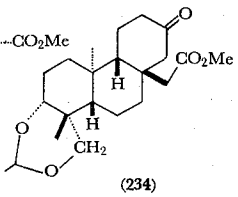

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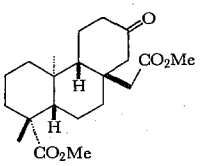

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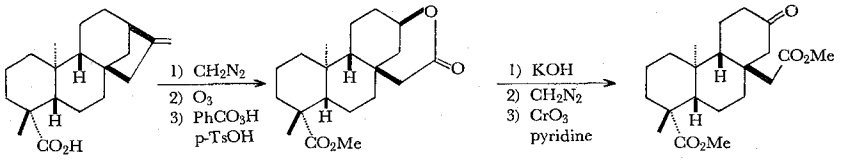
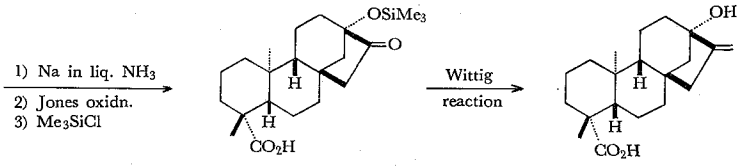
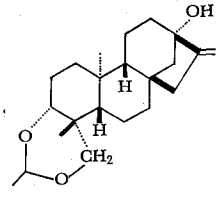




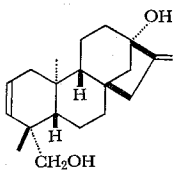
(236)

Chart 11

The synthesis of steviol (**236**) (Chart 11) and two A-ring modified analogs **237** and **238** was reported.[110]



(237)



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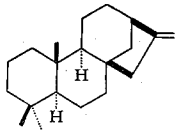


(239)

The full details of the synthesis of phyllocladene (**239**) from abietic acid was published.[111] The synthesis of *ent*-kaur-16-ene-11α, 15α-diol (**240**) and *ent*-kaur-16-en-15-on-11α-ol (**241**) from *ent*-kaur-16-ene was performed. The outline is shown in Chart 12.[112]

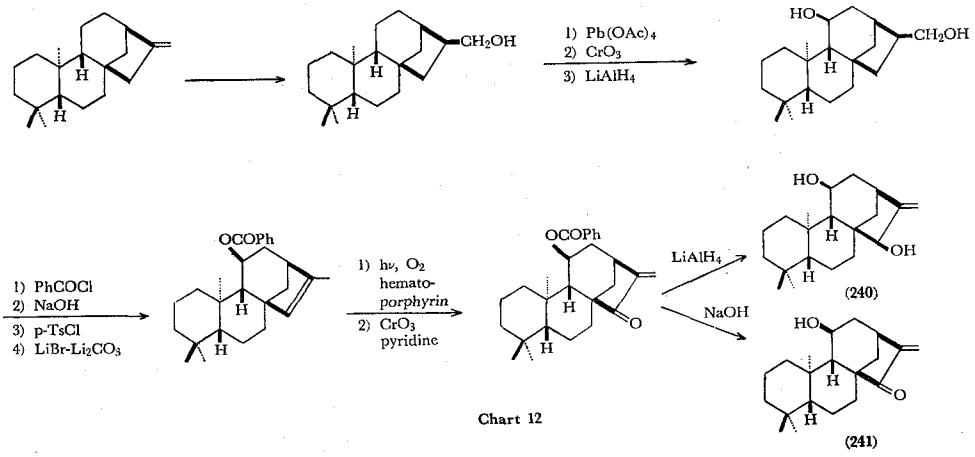
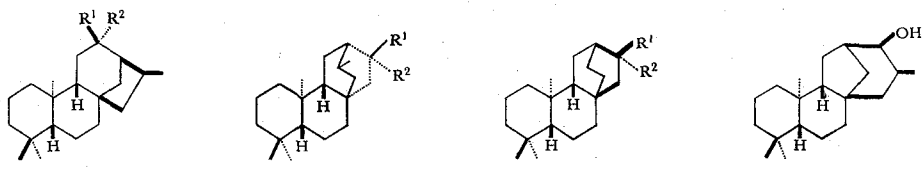


Chart 12

Buffered formolysis of *ent*-12α-*p*-tolylsulfonyloxykaurane (**242**) followed by hydrolysis gave chiefly the corresponding alcohol **243**, smaller amounts of the epimeric *ent*-atisan-13-(**244** and **245**) and 16-ols (**246** and **247**), together with traces of *ent*-kauran-12β-ol (**248**) and the *ent*-14(13→12)*abeo*-kauran-13α-ol (**249**).[113]



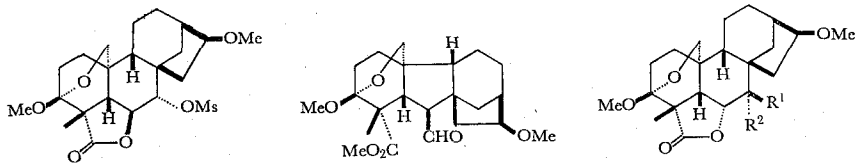
(242) R^1=OTs, R^2=H
(243) R^1=OH, R^2=H
(248) R^1=H, R^2=OH

(244) R^1=H, R^2=OH
(245) R^1=OH, R^2=H

(246) R^1=Me, R^2=OH
(247) R^1=OH, R^2=Me

(249)

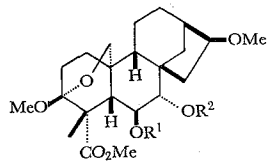
The detailed investigation on the ring B contraction of kauranolides and related compounds into gibberellane-type compounds was carried out. The lactone **250**



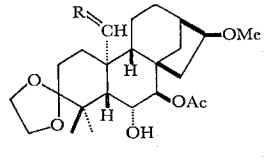
(250)

(251)

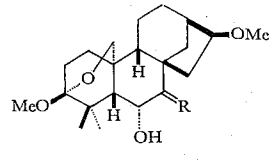
(252) R^1=OH, R^2=H
(254) R^1=H, R^2=OMs



(253) R^1=H, R^2=Ms
(255) R^1=Ms, R^2=Ac

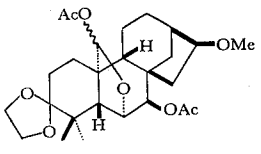


(256) R=H, OAc
(257) R=O

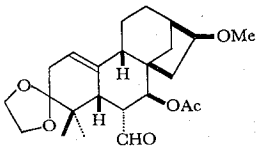


(258) R=α-H, β-OAc
(259) R=H_2
(260) R=α-OAc, β-H

on treatment with base and subsequent methylation gave the gibberellane aldehyde **251** and the alcohol **252**. The ester **253** gave a similar result. The lactone **254** on the same treatment afforded only the desired product **251** quantitatively. The ring B contraction did not proceed with the ester **255**. The results are rationalized in terms of stereochemical considerations.[114]



(261)



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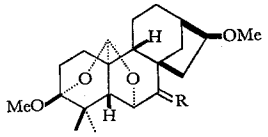
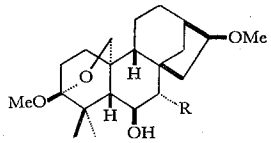
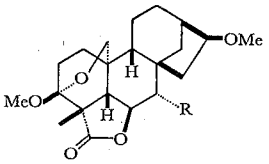


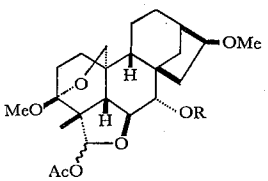
(263) R=α-H, β-OAc
(264) R=H_2
(265) R=α-OAc, β-H



(266) R=H
(267) R=OAc
(268) R=OMs



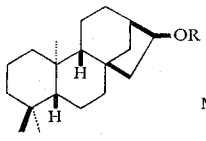
(269) R=H
(270) R=OAc



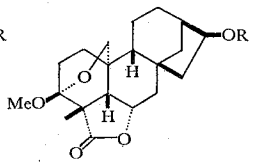
(271) R=Ac
(272) R=Ms

On the hypoiodite reaction, 17-norkauran-6α-ols **256**, **257**, **258**, **259**, and **260** gave **261**, **262**, **263**, **264**, and **265**, respectively. 17-Norkauran-6β-ols **266**, **267**, and **268** on the same reaction yielded **269**, a mixture of **270** and **271**, and **272**, respectively. Thus, the O-functionalization of the inactive C-19 methyl group of 17-norkauran-6-ols was achieved.[115]

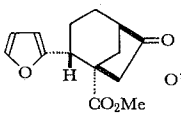
Treatment of *ent*-16α-methoxy-17-norkaurane (**273**) and lactone **274** with boron



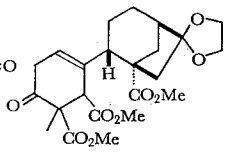
(273) R=Mc
(275) R=H



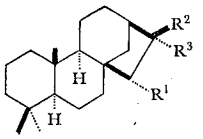
(274) R=Me
(276) R=H



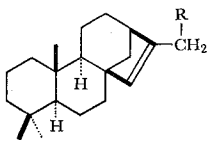
(277)



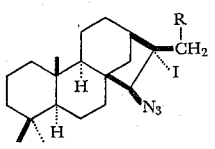
(278)



(279) R^1=H, R^2=CH_2I, R^3=N_3
(282) R^1=I, R^2=N_3, R^3=Mc



(280) R=H
(283) R=N_3



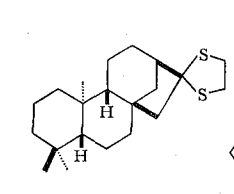
(281) R=H
(284) R=N_3

trifluoride-ether complex in ethanedithiol gave the corresponding alcohols **275** and **276**, respectively, with retention of the original stereochemisty.[116] Demethylfujenoic acid derivative **278** was synthesized from the key intermediate **277**.[117]

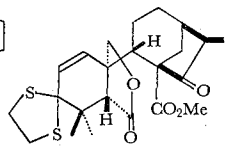
Reaction of sodium azide and iodine chloride with phyllocladene (**239**) gave the compound **279**. On the same treatment, isophyllocladene (**280**) gave two major products, **281** and **282**, and two minor products, **283** and **284**.[26]

Thioacetals **285**-**288** were dethioacetalized by the treatment with thallium (III) nitrate under mild conditions for a short time to recover the parent carbonyl compounds in good yields. The reaction mechanisms were also discussed.[118]

Oridonin (**289**), lasiokaurin (**290**), enmein (**291**), enmein-3-acetate (**292**), and related compounds (**293** and **294**), all of which have α-methylene cyclopentanone function in their molecule, were shown to have antitumor activity against Ehrlich ascites carcinoma inoculated into mice and specific activity against gram-positive bacteria. On the other hand, compounds **295** and **296**, trichokaurin (**297**), and dihydroenmein (**298**) showed any activity neither against tumor nor against bacteria. Thus it was concluded that the α-methylene-cyclopentanone system must be an important active center. Biomimetic reactions of oridonin and enmein with several thiols *etc.* supported this conclusion.[119,120]



(285)



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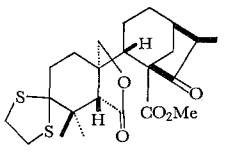

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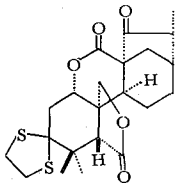

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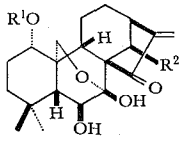
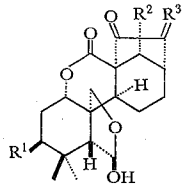
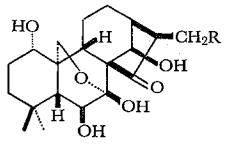


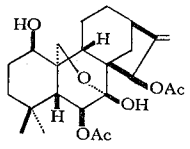
(289) R^1=H, R^2=OH
(290) R^1=Ac, R^2=OH
(293) R^1=R^2=H



(291) R^1=OH, R^2=H, R^3=CH_2
(292) R^1=OAc, R^2=H, R^3=CH_2
(294) R^1=H, R^2=OH, R^3=CH_2
(298) R^1=OH, R^2=H, R^3=α-Me, β-H



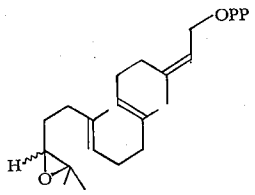
(295) R=H
(296) R=S$(CH_2)_3$Me



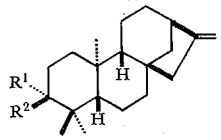
(297)

Enzymatic cyclization of *rac*-14,15-oxidogeranylgeranyl pyrophosphate (**299**) to hydroxykaurenes **300** and **301** was reported.[121] Conversion of geranylgeranyl pyrophosphate to *ent*-kaurene in enzyme extracts of sonicated chloroplasts was reported.[122] Incorporations of *ent*-kaur-16-ene and *ent*-kaur-16-en-15-one (**302**) into enmein (**291**) and oridonin (**289**) by *Isodon japonicus* were demonstrated by tracer experiments with seven labeled *ent*-kaurene derivatives. Furthermore, evidence was obtained that functionalization of *ent*-kaur-16-ene at the allylic C-15 atom proceeds through direct oxygenation.[123]

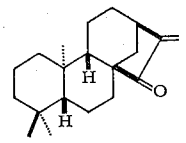
ent-Kaur-16-en-19-oic acid (**205**) was transferred by *Cunninghamella blakesleeana*



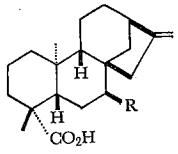
(299)



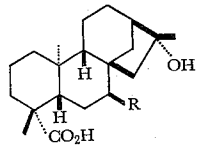
(300) R^1=OH, R^2=H
(301) R^1=H, R^2=OH



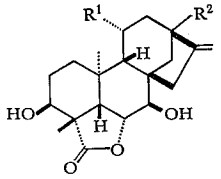
(302)



(205) R=H
(303) R=OH



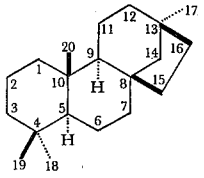
(304) R=H
(305) R=OH



(306) R^1=R^2=H
(307) R^1=OH, R^2=H
(308) R^1=H, R^2=OH

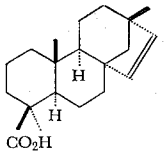
to a series of hydroxylated derivatives, **216**, **303**, **204**, and **305**.[124] Hydroxylation of 3β, 7β-dihydroxykaurenolide (**306**) by *Rhizopus arrhizus* afforded **307** and **308**.[125]

X. BEYERANE DERIVATIVES

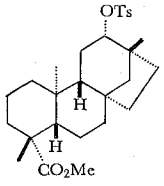


Beyerane

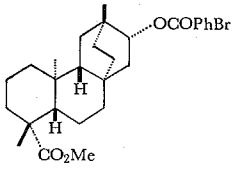
A new beyerane type diterpenic acid **309** accompanied by some new pimaran type diterpenes was isolated from *Dimorphotheca pluvialis*.[44] The X-ray analysis of methyl



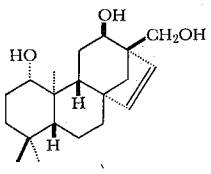
(309)



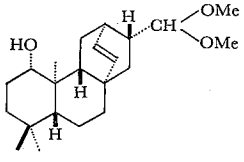
(310)



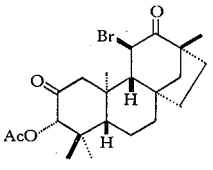
(311)



(312)



(313)

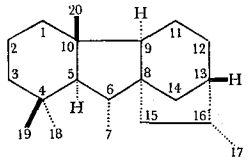


(314)

ent-16β-*p*-bromobenzyloxy-17(16→12)*abeo*-atisan-19-oate (**311**), a derivative of a formolysis product of methyl *ent*-12β-toluene-*p*-sulfonyloxybeyeran-19-oate (**310**), was reported.[126]

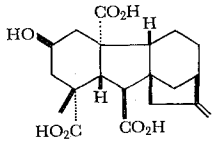
A minor product in the reaction of jativatriol (**312**) with hydrochloric acid was elucidated as **313** by the X-ray analysis.[127] The X-ray analysis of *ent*-3β-acetoxy–11α-bromobeyer-2, 12-dione (**314**) was reported.[128]

XI. GIBBERELLANE DERIVATIVES

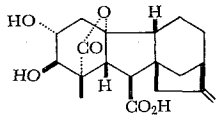


Gibberellane

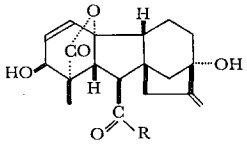
A general method for the conversion of 3-hydroxygibberellins into the methyl esters of 2-hydroxygibberellins was published. Thus the structures of two new gibberellins, GA_{46} (**315**) from seed of *Echinocystis macrocarpa* and GA_{47} (**316**) from cultures of *Gibberella fujikuroi* (strain GF-1a), were determined by these partial syntheses.[129]



(315)



(316)



(317) R=O–N(succinimide)

(318) R=NH-$CH_2C_6H_5$

(319) R=O-NH-$CO(CH_2)_2CONHCH_2C_6H_5$

The ^{13}C-NMR study of several gibberellin derivatives was reported.[130] The aminolysis of gebberellin-A_3-(N-hydroxy-succinimide)-ester (**317**) with benzylamine

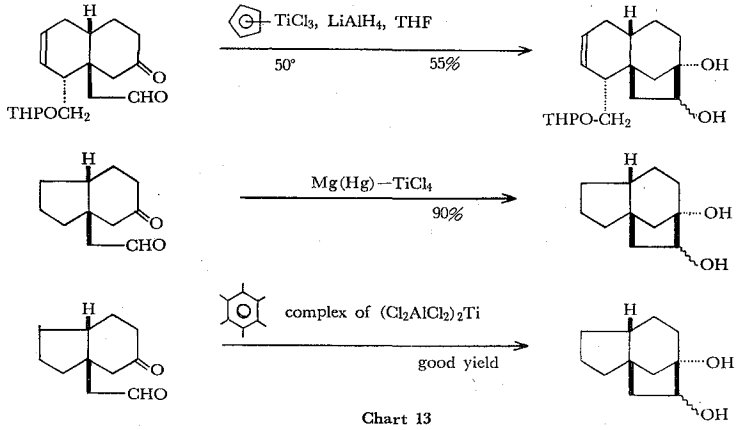
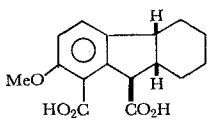


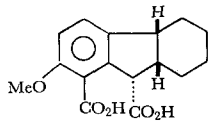
Chart 13

yielded gibberellin-A_3-benzylamide (**318**) and O-(gibberelin-A_3-oyl)-N-(benzylamino)-succinoyl-hydroxy-amine (**319**).[131] Three types of new reagents for the intramolecular pinacolic coupling of dicarbonyl compounds were developed. These are magnesium amalgam-titanium tetrachloride, cyclopentadienyltitanium trichloride-lithium aluminum hydride, and the hexamethylbenzene complex of the well-defined Ti (II) species $(Cl_2AlCl_2)_2Ti$.[132] These new pinacolic coupling reactions seem to be very effective for the construction of C-D ring system in synthesis of A_3-type gibberellins. (Chart 13)

A new stereocontrolled synthesis of some intermediates **11a** and **11b** for C_{20} gibberellins were published.[5] The reductive methylation of each epimeric diacid **320** and **321** was investigated by successive reaction with lithium in THF-liquid ammonia followed by methyl iodide. In each case, the diacid product (**322** from **320** and **323** from **321**) was formed by introduction of the C-4 methyl group from the side of the molecule opposite to the carboxyl group at C-6.[133]



(320)



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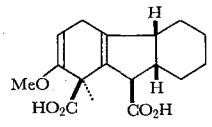
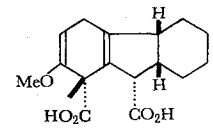
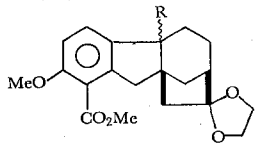


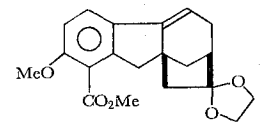
(322)



(323)



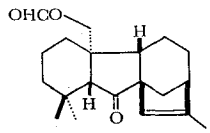
(324) R=α-H
(325) R=β-H



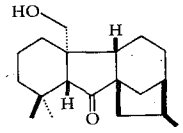
(326)

Various methods for the introduction of a carboxyl group into the benzylic position of compounds, **324**, **325**, and **326** were investigated. Among them, the best was found to involve deprotonation of these acetal esters with lithium N-cyclohexyl-N-t-butylamide, followed by carboxylation, which was highly stereoselective.[134]

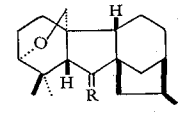
The hypoiodite reactions on the 7-norgibberellane derivatives were studied. The reaction with 7-nor-6-on-20-ol **328** derived from compound **327** afforded a high yield of 3,20-ether **329**. The second hypoiodite reaction with the α-ol **330** performed between C-6 and C-20 and yielded compound **331**, whose oxidation with the Jones reagent gave ketolactone **332**.[115]



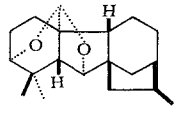
(327)



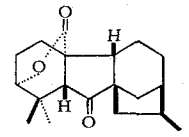
(328)



(329) R=O
(330) R=α-OH, β-H



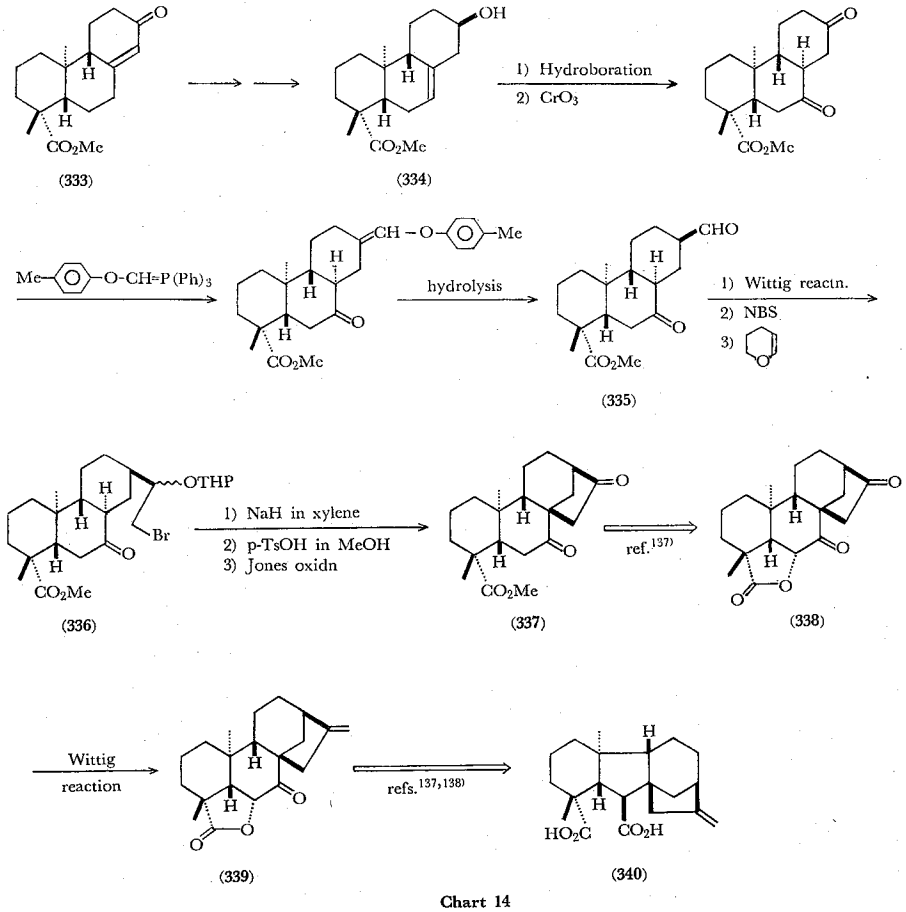
(331)



(332)

Ring B contraction of kauranoids and related compounds into gibberellane-type compounds was investigated in detail.[114] (See section IX.)

A formal total synthesis of *rac*-gibberellin A_{12} (**340**) mimicking the biogenetical pattern was achieved by employing methyl *rac*-7,16-dioxo-17-norkauran-19-oate (**337**) as a relay compound.[135,136] The outline is shown in Chart 14. Thus, compound **333** was converted into **337** *via* 7-en-13-ol **334**, 7-keto-13-al **335**, and a key intermediate **336** for ring D closure. Conversion of **337** into diketolactone **338** had been done.[137] Then the 16-oxo compound **338** was transformed into the 16-ene **339**, whose conversion into GA_{12} (**340**) had been performed.[137,138]

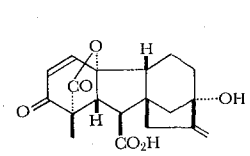


(333) (334) (335) (336) (337) (338) (339) (340)

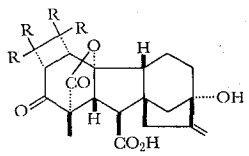
Chart 14

The photochemical [2+2]-cycloaddition of ethylene and tetramethyethylene to 3-dehydrogibberellin A_3 (**341**) under n→π^*-excitation conditions was investigated. The reaction lead to a 3:1 ratio of the *cis*-fused α- and β-cyclobutane annelated epimers **342** and **343** as well as **344** and **345** in 70 and 86% yield, respectively. Reduction of the annelated products with $NaBH_4$ was also discussed.[139]

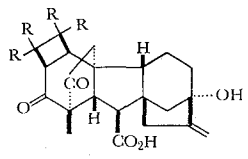
The structure and molecular packing of the cyclobutane annelated pseudogibberellin A_1 derivative **346**, prepared by trifluoroacetic acid catalyzed Wagner-Meer-



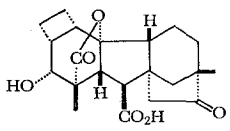
(341)



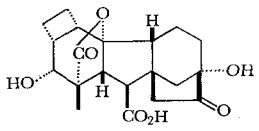
(342) R=H
(344) R=Me



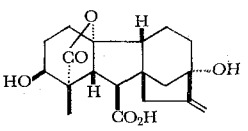
(343) R=H
(345) R=Me



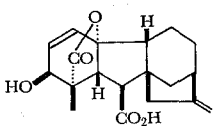
(346)



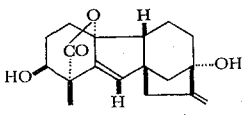
(347)



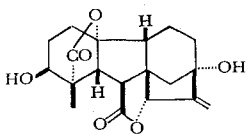
(348)



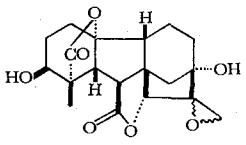
(349)



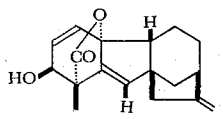
(350)



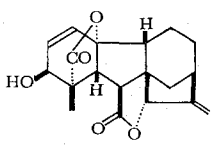
(351)



(352)

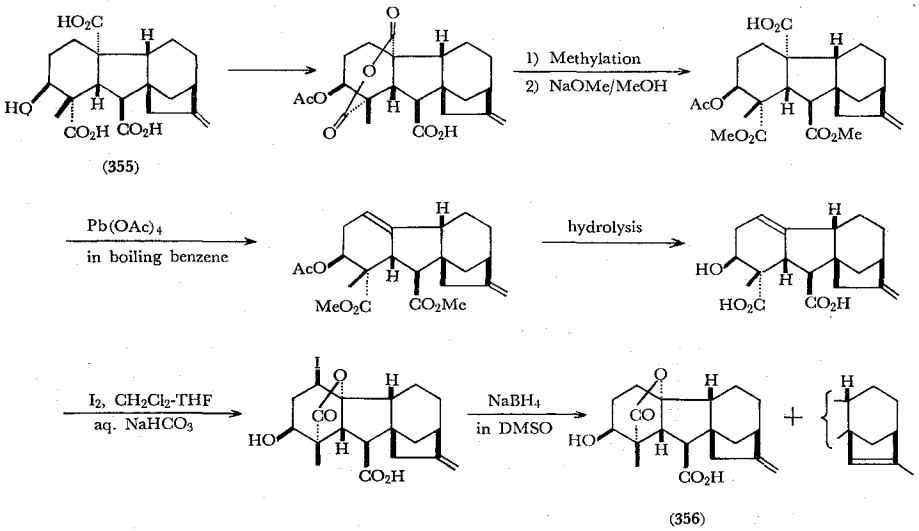


(353)



(354)

wein rearrangement of **347**, was established by X-ray analysis.[140] The oxidative lactonization and oxidative decarboxylation of gibberellin A_1 (**348**) and A_7 (**349**) with neutral manganese dioxide were investigated. The reaction with GA_1 gave compounds, **350**, **351**, and **352** and that with GA_7 produced **353** and **354**.[141]



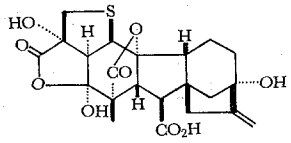
(355)

(356)

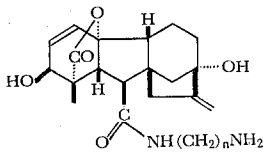
Chart 15

The synthesis of 2, 3-(^{3}H)-GA_9 with a specific activity of 47 Ci mmole^{-1} was reported.[142] The chemical conversion of GA_{13} (**355**) into GA_4 (**356**) was accomplished.[143] The route is shown in Chart 15.

The synthesis of gibberethione (**357**) isolated from seed of *Pharbitis nil* as a catabolic product of GA_3 was carried out by the direct coupling of 3-dehydro-GA_3 (**341**) and mercaptopyruvic acid.[144] The uniformly ^{3}H-labeled gibberellic acid (GA_3) amides, **358** and **359**, were prepared by amidation of the mixed anhydride of uniformly ^{3}H-labeled GA_3 and inactive GA_3 with $H_2N(CH_2)_nNH_2$ (n=4 and 5).[145]

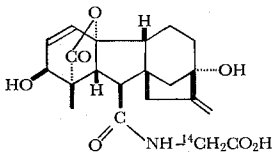


(357)

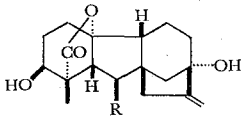


(358) n=4
(359) n=5

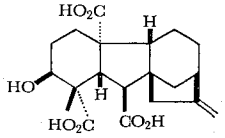
The synthesis of neutral and amino-substituted amides of the gibberellin A_3 and A_1 series *via* aminolysis of the corresponding gibberellin carboxylic acid anhydrides was published. The mass spectra and ^{1}H-NMR data of these compounds are also discussed.[146] The synthesis of gibberellin-A_3-oyl-2-^{14}C-glycine (**360**) was reported.[147] Gibberellin A_1-(7)-alcohol (**361**) and gibberellin-A_1-(7)-aldehyde (**362**) were prepared from GA_1 (**348**).[148]



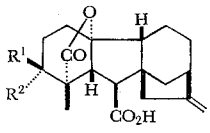
(360)



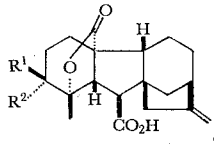
(361) R=CH_2OH
(362) R=CHO



(363)



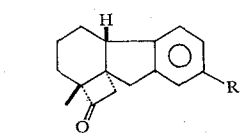
(364) R^1=OH, R^2=H
(366) R^1, R^2=O



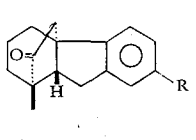
(365) R^1=OH, R^2=H
(367) R^1, R^2=O

GA_{13} (**363**), on treatment with $Pb(OAc)_4$-dimethylformamide (DMF) at 18°C, afforded a mixture (60:40) of the known GA_4 (**364**), identified by g.l.c.-mass spectrometry of the methyl ester, and the new isomeric lactone **365**; minor amounts of the corresponding 3-ketones **366** and **367** were also formed. This is the first chemical correlation of C_{20} gibberellin to C_{19} gibberellin.[149] A rearrangement of compounds **368** and **369** with triethyloxonium fluoroborate in CH_2Cl_2 into the corresponding bridged ketones **370** and **371** was published. Their transformation to some key hydrofluorene synthons **372** and **373** towards the C_{20} gibberellins was also reported.[150]

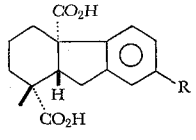
The photolysis of 3-dehydro-gibberellin A_1 (**374**) followed by methylation gave Δ^4-3.4-secoaldehyde **377** *via* acid **376**. The initial methylation of **374** followed by photolysis also gave **377**. The tetrahydro-compound **378** derived from **376** was treat-



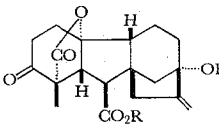
(368) R=H
(369) R=OMe



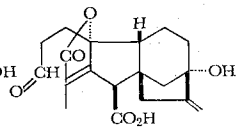
(370) R=H
(371) R=OMe



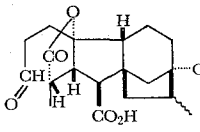
(372) R=H
(373) R=OMe



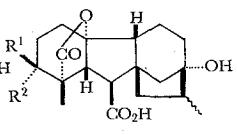
(374) R=H
(375) R=Me



(376) R=H
(377) R=Me



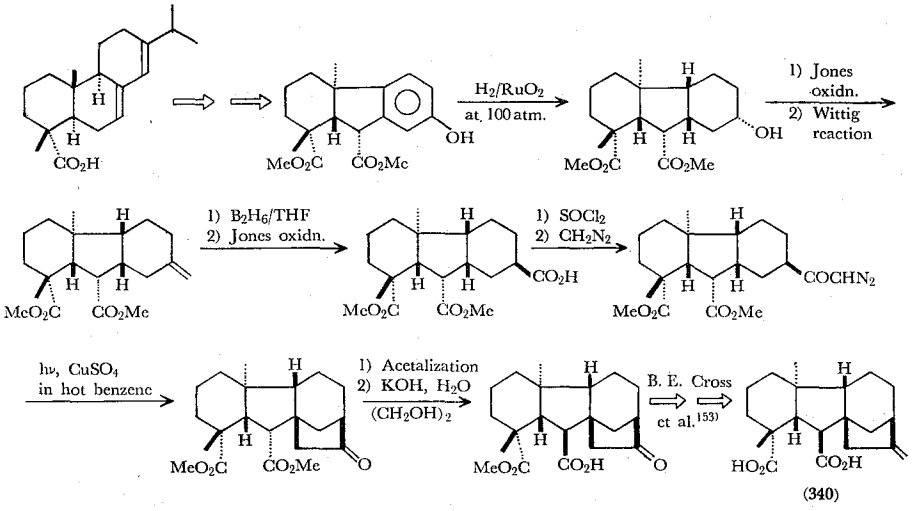
(378)
16-epimers



(379) R^1=OH, R^2=H
(380) R^1=H, R^2=OH

ed with alkali to yield epimeric alcohols **379** and **380**.[151] Thus, this reaction should be a good evidence for the retro-aldol mechanism to epimerization of the 3-hydroxy-group of GA_1 under the basic condition.

A formal synthesis of gibberellin A_{12} (**340**) was accomplished starting from *l*-abietic acid.[152] The synthetic route is summarized in Chart 16.

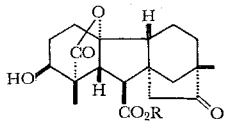


(340)

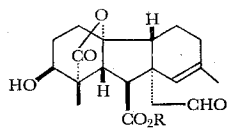
Chart 16

The n→π^* photolysis of gibberellin C (**381**) and its methyl ester (**382**) was performed by Norrish I cleavage to form secoaldehydes **383** and **384**, respectively. The subsequent intramolecular [2+2] cycloaddition of these secoaldehydes gave oxetane products **385** and **386**.[154]

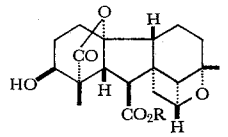
Isosteviol (**387**) and steviol acetate (**388**) were efficiently metabolized by cultures of resuspended mycelium of *Gibberella fujikuroi*, mutant B1-41a. Isosteviol was exclusively converted into ring-CD-rearranged derivatives (**389-392**) of gibberellins A_{17}, A_{19}, A_{20}, and 13-hydroxygibberellin A_{12}. Steviol acetate was mainly trans-



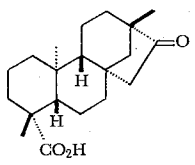
(381) R=H
(382) R=Me



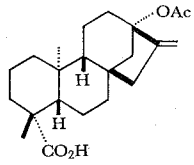
(383) R=H
(384) R=Me



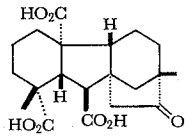
(385) R=H
(386) R=Me



(387)



(388)



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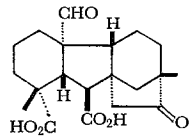

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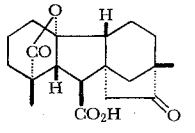

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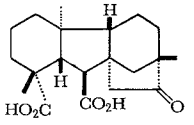
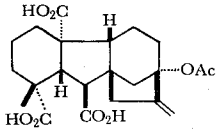
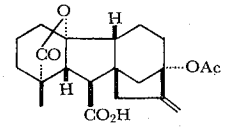


(392)



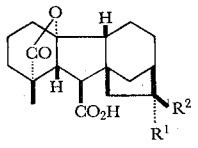
(393)



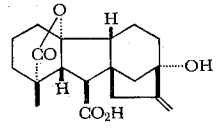
(394)

formed into the 7β-hydroxy- and 6β, 7β-dihydroy-derivatives and to the 13-acetates (**393** and **394**) of gibberellins A_{17} and A_{20}.[155]

Microbiological hydroxylation of gibberellin A_9 (**395**) and its methyl ester was investigated employing *Gibberella fujikuroi*, mutant B1-41a. Gibberellin A_9 was principally metabolized into gibberellins A_{20} (**396**) and A_{40} (**397**). Other metabolites were detected by g.l.c.-mass spectrometry. Gibberellin A_9 was partially metabolized by cultures of *Rhizopus nigricans* to give only gibberellin A_{10} (**398**). Gibberellin A_9 methyl ester, however, was converted into the methyl esters of the 16α- and 16β–epimers (**399** and **400**) of 16, 17-dihydro-16, 17-dihydroxygibberellin A_9, GA_{20} (**396**), GA_{40} (**397**), GA_{45} (**401**), and a monohydroxygibberellin A_9 (possibly **402**).[156]



(395) R^1, R^2=CH_2
(398) R^1=OH, R^2=Me
(399) R^1=OH, R^2=CH_2OH
(400) R^1=CH_2OH, R^2=OH



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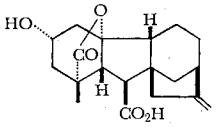
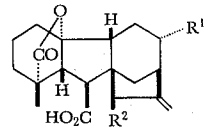
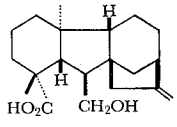


(397)



(401) R^1=H, R^2=OH
(402) R^1=OH, R^2=H

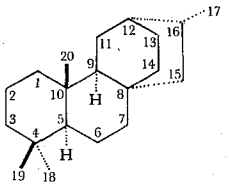


(403)

Origin of the oxygen atoms in the lactone bridge of C_{19}-gibberellins was studied. [^{18}O]-Label in the 19-oic acid of the C_{20} gibberellins, GA_{12} (**340**) and GA_{12}-alcohol (**403**), was incorporated without loss into C_{19}-gibberellins by cultures of *Gibberella fujikuroi*, mutant B1-41a.[157] Biological activities of fluorogibberellins and interactions with unsubstituted gibberellins were examined.[158] A Japanese review,

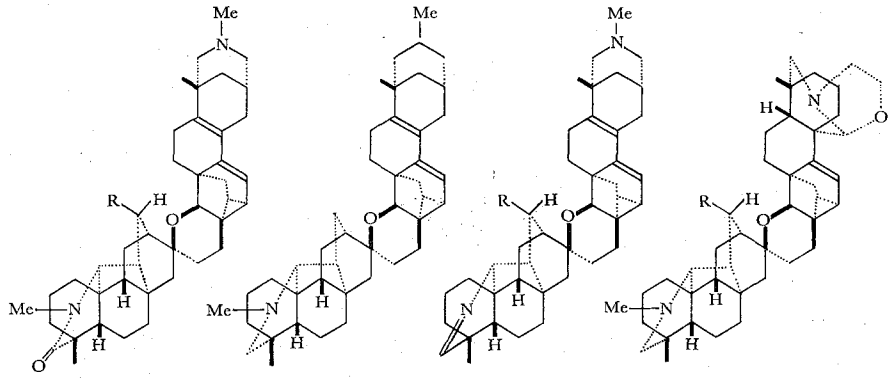
whose title is "Recent advances of biosynthetic study of gibberellins", was published.[159] In a Japanese review on the inhibitors against isoprenoids biosyntheses, a biosynthetic route of gibberellin A_3 was briefly illustrated.[160] A review "Studies on gibberellins in higher plants" was published in Japanese.[161]

XII. ATISANE DERIVATIVES



Atisane

The structures of staphigine (**404**) and staphirine (**405**), two novel bisditerpene alkaloids from *Delphinium staphisagria*, were established utilizing ^{13}C and ^{1}H NMR spectroscopy.[162] The structure elucidation of three novel alkaloids from *D. staphisagria*, staphidine (**406**), staphinine (**407**), and staphimine (**408**), was accomplished.[163] Staphisagnine (**409**) and staphisagrine (**410**), two new bis-diterpene alkaloids, were isolated from the mother liquors of the same plant.[164]



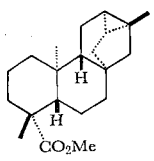
(**404**) R=OMe
(**405**) R=H

(**406**)

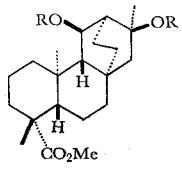
(**407**) R=OMe
(**408**) R=H

(**409**) R=OMe
(**410**) R=H

The molecular structure of a minor product of oxidative cleavage of methyl *ent*-trachyloban-19-oate (**411**) with thallic acetate was determined as **412** by the X-ray analysis of the corresponding diol **413**.[165]



(**411**)



(**412**) R=Ac
(**413**) R=H

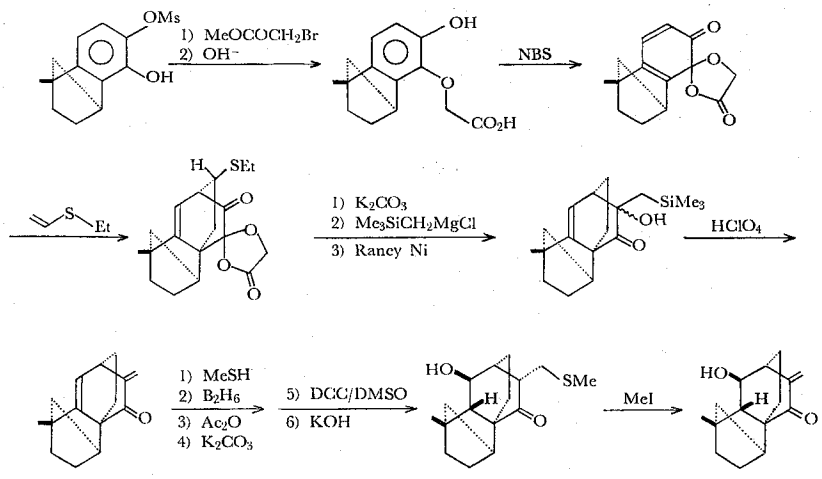
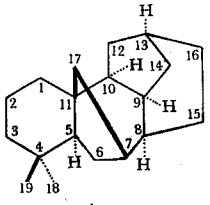


Chart 17

The construction of the substituted denudatine system by diene addition was reported.[166] The outline is shown in Chart 17.

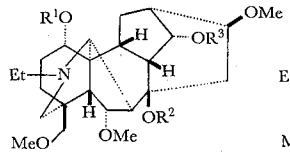
Two papers which were interesting for synthesis of atisane type diterpene alkaloids were published.[6,7]

XIII. ACONANE DERIVATIVES

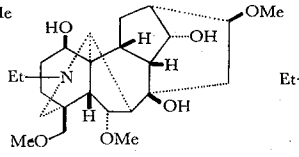


Aconane

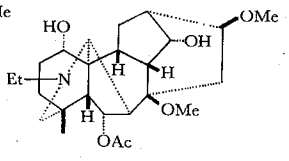
A new alkaloid, delphisine (**414**) was isolated from *Delphinium staphisagria*. Neoline (**415**) was prepared from delphisine (**414**) by several routes. Thus, 1α-hydroxy group of neoline was supported, and the revised structure **416** assigned by Marion



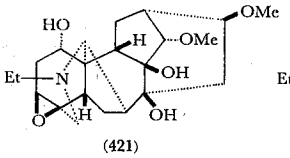
(414) R^1=H, R^2=R^3=Ac
(415) R^1=R^2=R^3=H
(417) R^1=Me, R^2=R^3=H
(418) R^1=R^2=Me, R^3=H
(419) R^1=Me, R^2=H, R^3=COPh



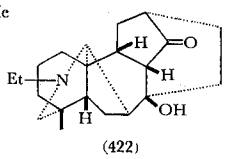
(416)



(420)



(421)



(422)

et al.[167] was proved to be in error. On the basis of other well-established chemical correlations, the structures of chasmanine and homochasmanine must also be revised to **417** and **418**, respectively.[168] Furthermore, the structure of chasmanine was established by an X-ray analysis of chasmanine 14α-benzoate (**419**) hydrochloide.[169]

A new alkaloid whose structure was elucidated as **416** was isolated from the same plant source.[170] Structure **420** was assigned to alkaloid A isolated from *Delphinium bicolor* by the examination of its ^{13}C NMR spectrum.[171] The structure and absolute configuration of excelsine (**421**) was determined by an X-ray analysis of its hydroiodide.[172] The X-ray analysis of the compound **422** which was synthesized from atisine was reported.[173]

An important intermediate **423** for the total synthesis of chasmanine (**417**) was synthesized as shown in Chart 18.[174]

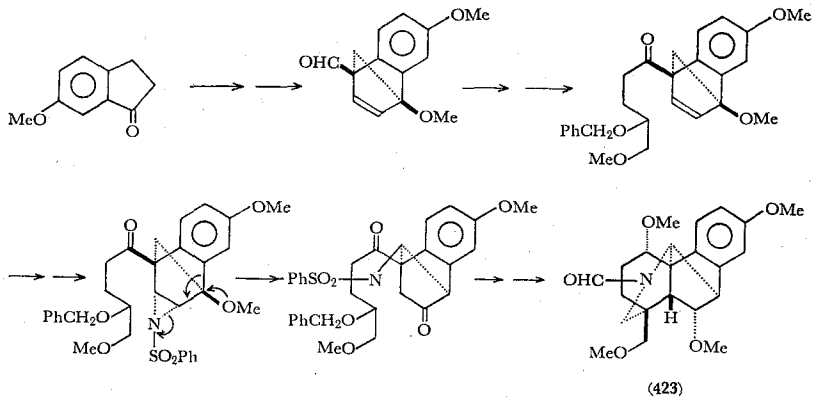
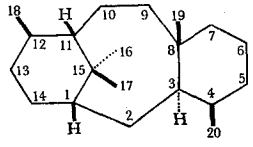


Chart 18

In a review article titled "the diterpenoid alkaloids of *Delphinium staphisagria*" was described the chemistry of aconane type alkaloids together with other alkaloids.[175]

XIV. TAXANE DERIVATIVES

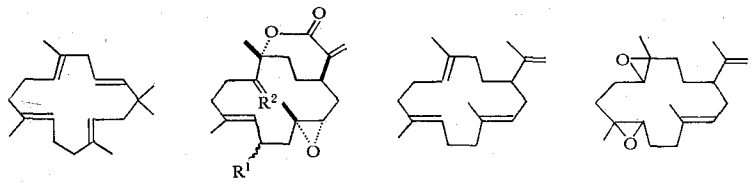


Taxane

No papers have been published on the title topics in 1976.

XV. THE OTHERS

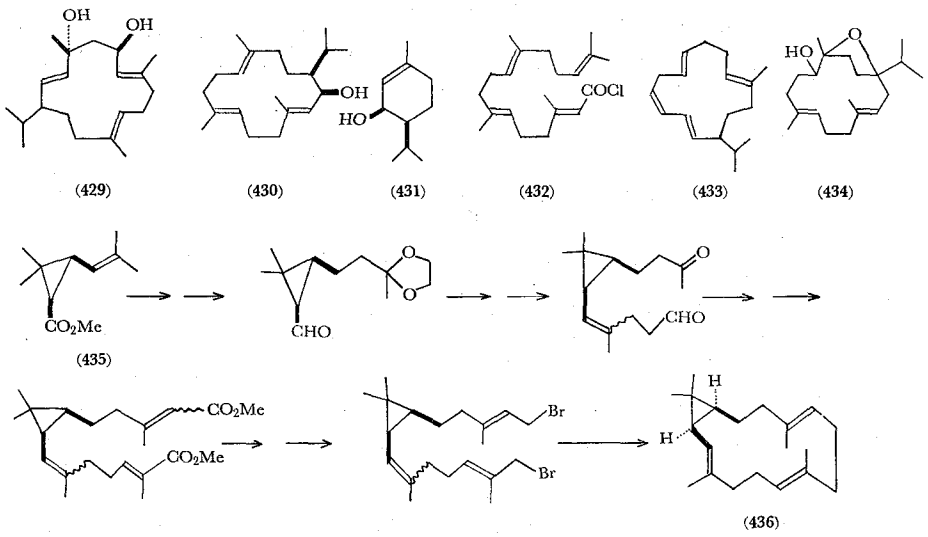
New diterpenes, flexibilene (**424**),[176] 6-hydroxysinulariolide (**425**), 11-dehydrosinulariolide (**426**), (E)-(−)-cembrene A (**427**), and 3, 4: 11, 12-diepoxycembrene A (**428**) were isolated from the soft coral, *Sinularia flexibiles*, as the minor diterpenoids.[177]



(424) (425) R^1=OH, R^2=α-H, β-OH (426) R^1=H, R^2=O (427) (428)

Duva-4, 8, 13-triene-1, 3-diol (**429**) found in the leaf wax of *Nicotiana tobacum* was shown to have highest concentration in the wax from young leaves and quantitatively decrease in importance with leaf age.[178] Absolute stereochemistry of mukulol (**430**) was determined by chemical correlation with cembrene A (**427**) and (+)-*cis*-piperitol (**431**).[179]

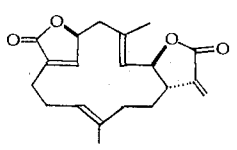
The biogenetic type cyclization of geranylgeranic acid chlorid (**432**) followed by a series of reactions *via rac*-mukulol (**430**) afforded *rac*-cembrene (**433**).[180] *rac*-Incensole (**434**) was also synthesized from *rac*-mukulol (**430**).[181] A total synthesis of casbene (**436**) from methyl *rac-cis*-chrysanthemate (**435**) was accomplished.[182] The outline is shown in Chart 19.



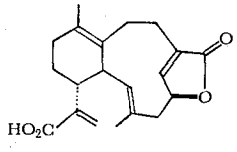
(429) (430) (431) (432) (433) (434) (435) (436)

Chart 19

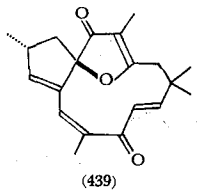
Jones oxidation of cembrene (**433**) has been carried out and the products were analyzed in detail.[183] The conformation and relative stereochemistry of ovatodiolide (**437**) isolated from *Anisomeles ovata* were studied by ^{1}H NMR spectroscopy. X-ray analyses were also done to confirm the structures of ovatodiolide (**437**) and acid cyclization product **438**.[184] The molecular structure and absolute configuration of jatrophone (**439**),[185] *p*-iodobenzoate (**440**) of jeunicin isolated from *Eunicea mammosa*,[186] and new thunberganoid **441**[187] were determined by the X-ray analysis.



(437)



(438)



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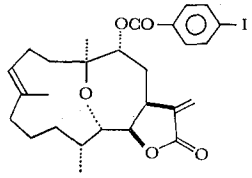

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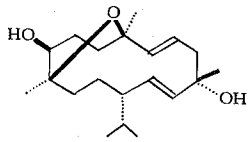
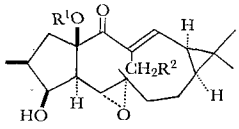


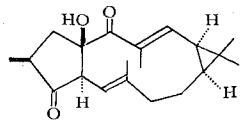
(441)

Four new diterpenes, jolkinols A (**442**), B (**443**), C (**444**), and D (**445**), were isolated from *Euphorbia jolkini*.[188] The structures of dictyol A (**446**) and B (**447**) isolated from the brown alga, *Dictyota dichotoma*, were determined on the bases of spectroscopic and chemical evidence.[189] These diterpenes were also isolated from the digestive gland of the molluscs, *Aplysia depilans*.[190] Independent examination of the constituents of the red alga, *Sphaerococcus coronopifolius*, by two groups led to the isolation of closely related diterpenes, sphaerococcenol A (**448**)[191] and bromosphaerol (**449**).[192]

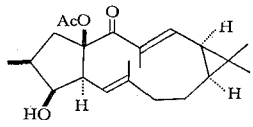
Uniquely different class of diterpenes were isolated from the marine animal



(442) R^1=cinnamoyl, R^2=OH
(443) R^1=cinnamoyl, R^2=H



(444)



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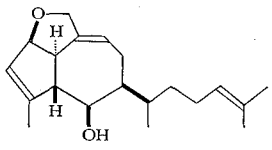

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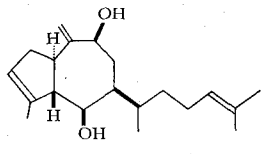
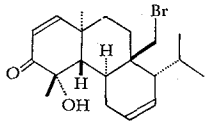


(447)



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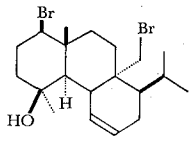

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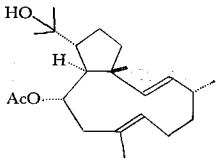
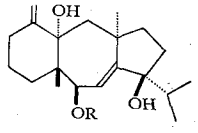
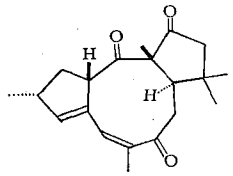


(450)

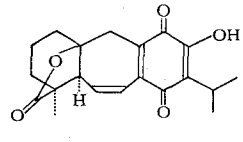


(451) R=H
(452) R=OAc

sources. One of them was isolated from *Dollabella californica* and assigned structure **450**.[193] Dolatriol (**451**) and dolatriol 6-acetate (**452**) were isolated from *Dollabella auricularia*.[194] The structure of jatrophatrione (**453**), a constituent of the chloroform extract of *Jatropha macrorhiza*, was determined by an X-ray analysis.[195] It was found to possess inhibitory activity toward the P-388 lymphocytic leukemia test system. The structure of icetexone (**454**) isolated from *Salvia ballotaeflorae* was determined from diffractometer data by direct methods.[196] Furthermore, X-ray analyses were effectively used for determination of several new diterpenes, 18-hydroxydecipia-2(4), 14-dien-1-oic acid (**455**) from *Eremophila decipiens*,[197] gnidimacrin (**456**) and its 20–palmitate (**457**), macrocyclic antileukemic diterpenoid esters from *Gnidia subcordata*[198], cinnzeylanine (**458**) and cinnzeylanol (**459**) from *Cinnamonum zeylanicum*,[199] and prostratin (**460**) from *Pimelea prostrata*.[200]



(453)



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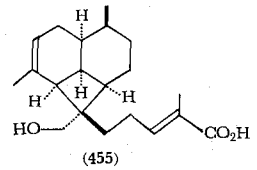
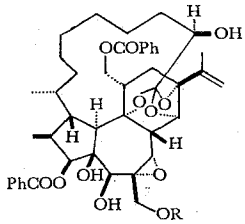
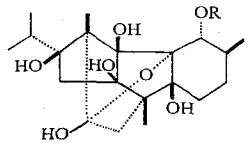


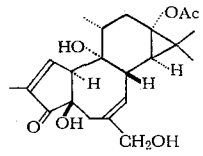
(455)



(456) R=H
(457) R=$COC_{15}H_{31}$

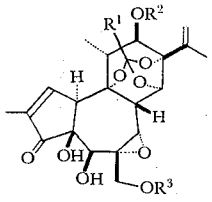


(458) R=Ac
(459) R=H

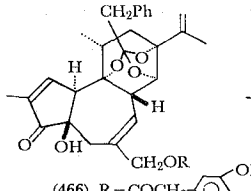


(460)

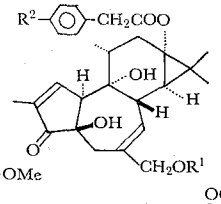
Chemical evidence for prostratin (**460**) was given by Hecker *et al.*[201] The new potent antileukemic principles, gnidilatin 20-palmitate (**461**), gnidilatidin 20-palmitate



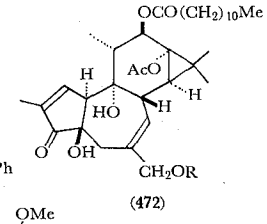
(461) $R^1=(CH_2)_8Me$, $R^2=COPh$, $R^3=COC_{15}H_{31}$
(462) $R^1=CH=CH-CH=CH(CH_2)_4Me$, $R^2=COPh$, $R^3=COC_{15}H_{31}$
(463) $R^1=(CH_2)_8Me$, $R^2=COPh$, $R^3=H$
(464) $R^1=CH=CHCH=CH(CH_2)_4Me$, $R^2=COPh$, $R^3=H$
(465) $R^1=(CH_2)_8Me$, $R^2=Ac$, $R^3=H$



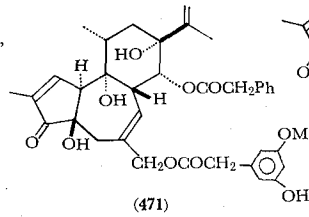
(466) R=$COCH_2$-(OMe, OH)
(467) R=$COCH_2$-(OH)



(468) $R^1=R^2=H$
(469) $R^1=Ac$, $R^2=H$
(470) $R^1=Ac$, $R^2=OH$



(472)



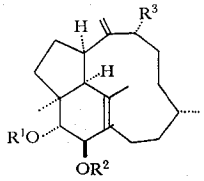
(471)

R=$COCH_2(CH_2)_5(CH_2CH=CH)_3Et$

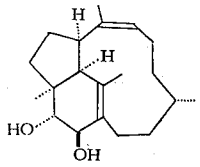
(**462**), and gnidilatin (**463**), and the new toxic diterpenoids, gnidilatidin (**464**) and gnidiglaucin (**465**) were isolated from *Gnidia* species.[202] Gnidilatidin (**464**) was independently isolated from *Daphne odora* as a nematicidal constituent named odoracin.[203]

From the resin isolated from latex of *Euphorbia poisonii* in Nigeria, four diterpenenoids, **466-469**, were isolated. Among these, **467** and **468** were new natural products.[204] The dried latex of the same plant was exhaustively extracted with acetone, from which compounds **470** and **471** were isolated.[205] A new cryptic irritant and cocarcinogen **472** was isolated from seeds of *Croton sparciflorus*.[206]

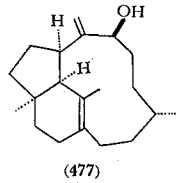
The structure of TG-2 (**473**), one of the major constituents of the soldier secretions of *Tinervitermes gratiosus*, was determined by an X-ray analysis.[207] Five other congeners TG-1 (**474**), TG-3 (**475**), and TG-4 (**476**) from *T. gratiosus*, TB-1 (**477**) and TB-3 (**478**) from *T. bettonianus*, were isolated and their structures were elucidated from spectral studies.[208] TG-1 was identical with TB-2 isolated from *T. bettonianus*.



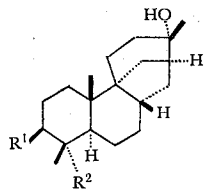
(**473**) $R^1=R^2=H$, $R_3=OAc$
(**474**) $R^1=R^2=R^3=H$
(**476**) $R^1=R^2=Ac$, $R^3=OH$



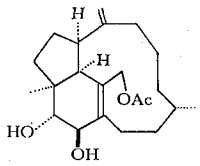
(**475**)



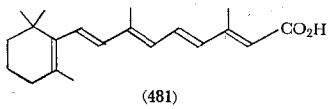
(**477**)



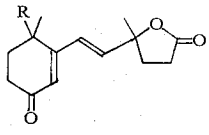
(**479**) $R^1=OH$, $R^2=Me$
(**480**) $R^1=H$, $R^2=CH_2OH$



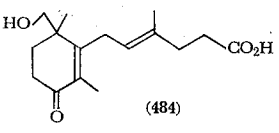
(**478**)



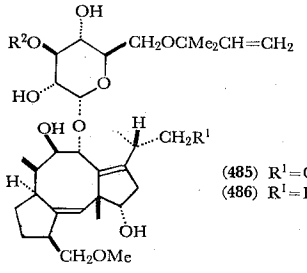
(**481**)



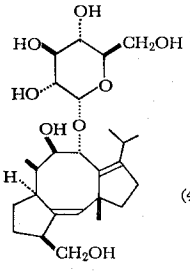
(**482**) R=Me
(**483**) $R=CH_2OH$



(**484**)



(**485**) $R^1=OAc$, $R^2=Ac$
(**486**) $R^1=R^2=H$

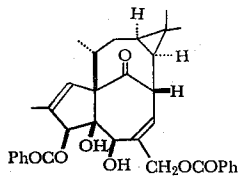


(**487**)

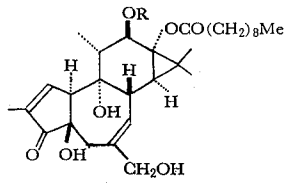
Two new diterpenes, maritinol (**479**) and stemodinol (**480**), were isolated from *Stemodia maritima*.[209] After the intraperitoneal administration of retinoic acid (**481**) to rats, three urinary metabolites **482**, **483**, and **484** were isolated and identified.[210]

Biosynthetic studies of fusicoccin (**485**) and fusicoccin J (**486**) and H (**487**) using [3-^{13}C]mevalonic acid lactone revealed that a polyprenyl pyrophosphate precursor cyclizes in a manner different to that previously observed in the biosynthesis of the ophiobolins.[211]

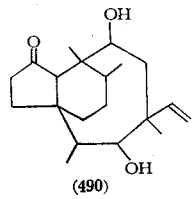
Ingenol 3, 20-dibenzoate (**488**) and phorbol 12-tiglate 13-decanoate (**489**) were isolated from *Euphorbia esula* and *Croton tiglium*, respectively and characterized as antileukemic components.[212] A number of derivatives of pleuromutilin (**490**) were prepared[213,214] and bactericidol activity of some derivatives were tested.[213] The structural relationship of phorbol-12-myristate-13-acetate and cortisol was discussed and a possible mechanism for the tumor promoting activity of phorbol was presented.[215]



(488)



(489) R=CO(Me)C=CHMe



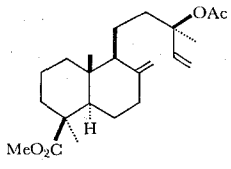
(490)

Many kinds of diterpene resin acids were isolated from *Pinus densiflora* needles and cortex.[216] Isolation of free *cis*- and *trans*-phytol from the red alga *Gracilaria andersoniana* was reported.[217]

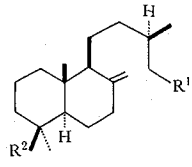
In a review titled "Diterpenoids of *Isodon* and *Teucrium* Plants", many kaurane- and clerodane-derivatives were described.[218] In a review titled "Biosynthetic Studies with ^{13}C-Labeled Precursors", examples on some diterpenoids, *e.g.* virescenol B, gibberellic acid, aphidicolin, and fusicoccin, were described.[56] Another review concerning the biosynthesis of isoprenoids appeared in Japanese.[219]

ADDENDUM TO III.

The bled resin of *Araucaria imbricata* (*A. araucana*) was examined and nine labdane derivatives, **491-499**, were isolated.[220] Among them, compounds **492, 495,** and **497** had been reported.



(491)



(492) R^1=CH_2OAc, R^2=CO_2Me
(493) R^1=CH_2OH, R^2=CO_2Me
(494) R^1=CO_2Me, R^2=Me
(495) R^1=R^2=CH_2OH
(496) R^1=CH_2OH, R^2=Me
(497) R^1=CH_2OAc, R^2=CHO
(498) R^1=CH_2OH, R^2=CHO
(499) R^1=CH_2OAc, R^2=Me

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